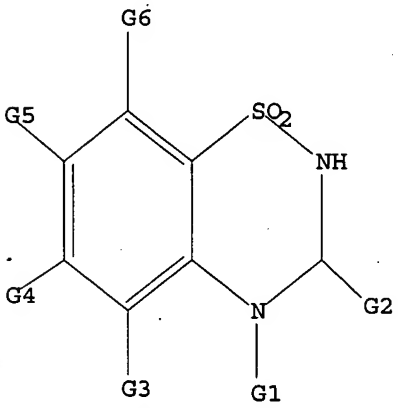
Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
12:CLASS 15:CLASS 17:CLASS 18:CLASS 21:CLASS 24:CLASS

1

L1 STRUCTURE UPLOADED

=> d l1
L1 HAS NO ANSWERS
L1 STR



G1 H,Ak,Cb,C

G2 H,Cb,Ak,C,O,CH2,CH,Hy

G3 H,Cb,Ak,SO2,X

G4 NH,N,Cy

G5 S,NH,Ak,SO2,Cy

G6 H,CN,NO2,C,O,S,SO2,NH,X,Cy,Ak

Structure attributes must be viewed using STN Express query preparation.

=> s l1
SAMPLE SEARCH INITIATED 12:44:03 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 656 TO ITERATE

100.0% PROCESSED 656 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11584 TO 14656
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 12:44:12 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 13037 TO ITERATE

100.0% PROCESSED 13037 ITERATIONS 37 ANSWERS
SEARCH TIME: 00.00.01

L3 37 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'CAPLUS' ENTERED AT 12:44:17 ON 03 NOV 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907 - 3 Nov 2006 VOL 145 ISS 19
FILE LAST UPDATED: 1 Nov 2006 (20061101/ED)

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=> s l3
L4 33 L3

=> d ibib abs hitstr tot

own work

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

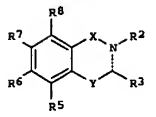
ACCESSION NUMBER: 1999:549265 CAPLUS
DOCUMENT NUMBER: 131:184974
TITLE: Preparation of benzothiadiazines, quinazolines, and other aryl-fused heterocycles as positive AMPA-receptor modulators for treatment of memory and learning disorders
INVENTOR(S): Gouliaev, Alex Haahr; Larsen, Mogens; Varming, Thomas; Mathiesen, Claus; Johansen, Tina Holm; Scheel-Kruger, Jorgen; Olsen, Gunnar M.; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

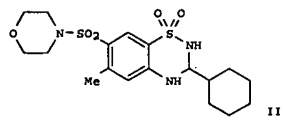
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942456	A2	19990826	WO 1999-DK70	19990218
WO 9942456	A3	19991007		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9609414	A	19970612	ZA 1996-9414	19961108
CA 2320354	AA	19990826	CA 1999-2320354	19990218
AU 9925123	A1	19990906	AU 1999-25123	19990218
AU 751384	B2	20020815		
ZA 9901301	A	19990913	ZA 1999-1301	19990218
TR 200002427	T2	20010122	TR 2000-200002427	19990218
EP 1071426	A2	20010131	EP 1999-904730	19990218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002504481	T2	20020212	JP 2000-532408	19990218
EE 200000468	A	20020415	EE 2000-468	19990218
RU 2214405	C2	20031020	RU 2000-121882	19990218
NO 2000004121	A	20001017	NO 2000-4121	20000817
US 6943159	B1	20050913	US 2000-641814	20000818
US 2004043987	A1	20040304	US 2003-642224	20030818

PRIORITY APPLN. INFO.:
DK 1998-226 A 19980218
WO 1999-DK70 W 19990218
US 2000-641814 A3 20000818

OTHER SOURCE(S): MARPAT 131:184974
GI

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)


I


II

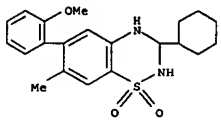
AB Benzothiadiazines, quinazolines, and other aryl-fused heterocycles (I) [wherein the bond represented by the broken line may be a single, double bond, or absent; and if the bond is absent, then the N is substituted with a H and R2; X = SO2, CO, or CH2; Y = -CH(R4)-, -N(R4)-, -N(R4)-CH2-, or O; R2, R4 = H, alkyl, cycloalkyl, aryl, benzyl, substituted carbonyl, or taken together with R3 = (un)substituted 4-7 membered ring; R3 = H, (un)substituted cycloalkyl, (un)substituted alkyl, (un)substituted alkoxy, acyl, or taken together with R2 or R4 = (un)substituted 4-7 membered ring, etc.; R5 = H, halogen, alkyl, alkenyl, alkynyl, aryl, or (un)substituted sulfonamido; R6, R7, R8 = H, halogen, (un)substituted alkyl, CN, cyanoalkyl, NO2, (un)substituted alkoxy, (un)substituted sulfonamido, (un)substituted aryl, etc.] were prepared as pos. AMPA-receptor modulators for treatment of memory and learning disorders. Thus, ClSO2NCO was added to a cooled solution of m-toluidine and nitroethane or nitromethane followed by addition of AlCl3 and reaction with H2SO4 to form a mixture of 2-amino-6-methylbenzenesulfonamide and 2-amino-4-methylbenzenesulfonamide. The latter isomer was separated by recrystn. and cyclized with cyclohexanecarbonyl chloride in a mixture of TEA, 4-(N,N-dimethylamino)pyridine, and THF to yield dihydro-3-cyclohexyl-6-methyl-1,2,4-benzothiadiazine-1,1-dioxide. The dihydrobenzothiadiazine-1,1-dioxide was chlorosulfonated with chlorosulfonic acid, sulfamoylated with morpholine, and reduced with DIBALH in toluene to give 3-cyclohexyl-6-methyl-7-morpholinosulfonyl-1,2,3,4-tetrahydro-1,2,4-benzothiadiazine-1,1-dioxide (II). Selected compds. of the invention were tested for in vitro inhibition of 3H-AMPA binding and exhibited IC50 values ranging from 3.4 μM to 45 μM. Two compds. were tested and showed significantly increased potentiation of AMPA-induced [3H]GABA release from cultured cortical neurons relative to the potentiation induced by 30 μM cyclothiazide. Expts. were performed in voltage clamp, and all tested compds. reversibly potentiated the current induced by application of 30 μM AMPA. The results of iontophoretic application showed that cyclothiazide did not exhibit any in vivo effects after i.v. administration but that five compds. of the invention enhanced AMPA evoked spike activity in an activity-dependent manner. Passive avoidance expts. were performed to test the pharmacol. effect of compds. on associative

L4 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

memory. Mean entry latency results for each group and the memory enhancing effect of different concns. of one compd. were given.

IT 240139-62-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiadiazines, quinazolines, and other aryl-fused heterocycles as pos. AMPA-receptor modulators for treatment of memory and learning disorders)

RN 240139-62-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 3-cyclohexyl-3,4-dihydro-6-(2-methoxyphenyl)-7-methyl-, 1,1-dioxide (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:525846 CAPLUS
DOCUMENT NUMBER: 113:125846
TITLE: Evaluation of partition coefficient of chemical substance
INVENTOR(S): Miyagawa, Masami; Hanai, Masasuke
PATENT ASSIGNEE(S): Fuji Photo Film Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

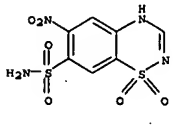
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 02016448	A2	19900119	JP 1988-167181	19880704

PRIORITY APPLN. INFO.:
JP 1988-167181 19880704

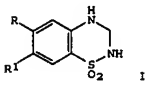
AB The partition coefficient of chemical substances with a ring containing no saturated C is evaluated by the log P = log Padditive + Σiαi(Σj≠i πj') + Σi ρi(Σj≠i σj) + ΣFi,j,... [P = partition coefficient of chemical substance; π = changes in log of partition coefficient when an atomic group is substituted on the aromatic ring; π' = contribution from partial atomic units within the distance of n (n = number of bonds from the substitution position; 1 ≤ n ≤ 10); α = criterion for changing π' by one atomic group; σ = elec. substitution constant; ρ = criterion for changing π corresponding with σ; F = changes in log of partition coefficient when > 2 atomic groups are substituted; log Padditive = (sum of log of partition coeffs. of each atomic groups) + (correction factor for bond and branch of polar group); i, j = number of atomic group].

IT 23141-81-3
RL: PRP (Properties); ANST (Analytical study)
(evaluation of partition coefficient of)

RN 23141-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



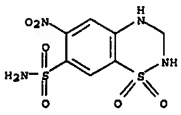
L4 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1983:569045 CAPLUS
DOCUMENT NUMBER: 99:169045
TITLE: Quantum-chemical and physicochemical properties of hydrochlorothiazide
AUTHOR(S): Orita, Y.; Ando, A.; Yamabe, S.; Nakanishi, T.; Arakawa, Y.; Abe, H.
CORPORATE SOURCE: Med. Sch., Osaka Univ., Fukushima, Japan
SOURCE: Arzneimittel-Forschung (1983), 33(5), 688-91
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



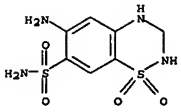
I

AB The electronic states of hydrochlorothiazide (I, R = Cl, R1 = NH2SO2-) [58-93-5] its related mols. I (R = 6th position and R1 = 7th position; R and R1 = Cl, H, CH3, CH3O, NO2, etc.) were obtained by CNDO/2, van der Waals volume and hydrophobic parameters of the substituent I (R = 6th position and R1 = 7th positions; R and R1 = Cl, H, CH3, CH3O, NO2, etc.) the 6th and 7th positions in the benzothiadiazine were estimated The results
are discussed from the viewpoint of the structure-activity relationship anal. Lower LUMO (LUMO level) of hydrochlorothiazide, predicted by the interated Hueckel's MO method, was confirmed by CNDO/2 calcn. The introduction of the sulfamoyl group of the 7th position in the benzothiadizine ring brought out a neg. formal charge at this position. The diuretic effect of substituents at the 6th position in the benzothiadiazine ring was analyzed with respect to their van der Waals vols. and hydrophobic parameters. Van der Waals vols. seemed to have a close relationship to the diuretic activity. The highest correlation coefficient of the regression equation for structure-activity relationship was
obtained using the formal charge of the 7th position in the benzothiadiazine ring, and the van der Waals volume and hydrophobic parameter of the substituent of the 6th position. A model for the action site of hydrochlorothiazide is proposed, consisting of a large lipophilic hole and an electrostatic interaction site in the tubular membrane.
IT 23141-88-0 86579-01-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(diuretic activity of, structure and quantum chemical in relation to)

L4 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 23141-88-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide
(6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1976:421483 CAPLUS
DOCUMENT NUMBER: 85:21483
TITLE: 3-Benzyl-7-sulfamyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide derivatives
INVENTOR(S): Klosa, Josef
PATENT ASSIGNEE(S): Fed. Rep. Ger.
SOURCE: Ger., 3 pp.
CODEN: GWXXAW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1570023	A	19691211	DE 1965-K55753	19650408
DE 1570023	B2	19760102		
DE 1570023	C3	19760826		

PRIORITY APPLN. INFO.: DE 1965-K55753 A 19650408

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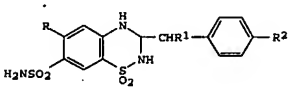

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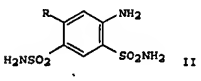
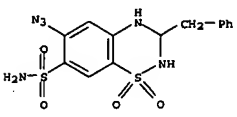
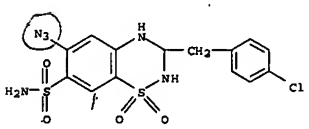


II

AB Benzothiadiazine dioxides I (R = Cl, CF3, N3, R1 = R2 = H; R = Cl, N3, R1 = H, R2 = Cl; R = Cl, R1 = Me, R2 = H) were prepared in 90-6% yield by condensing 4-R2C6H4CR1(OH)CH2OH with the disulfamoylanilines II.
IT 17984-63-3P 59521-78-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 17984-63-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(phenylmethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 59521-78-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-[(4-chlorophenyl)methyl]-3,4-dihydro-, 1,1-dioxide (9CI) (CA INDEX NAME)

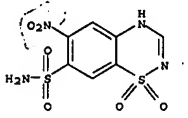


L4 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1969:45864 CAPLUS
DOCUMENT NUMBER: 70:45864
TITLE: Structure-activity relations among the thiazide diuretics
AUTHOR(S): Novello, Frederick C.; Sprague, James M.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab. Div., Merck and Co., Inc., West Point, PA, USA
SOURCE: Industrie Chimique Belge (1967), 32(Spec. No.), 222-5
CODEN: ICBEAJ; ISSN: 0019-9052
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Acidity, lipid solubility, carbonic anhydrase inhibition, and diuretic potency of 41 thiazides were examined Conversion of a thiazide to a hydrothiazide results in an increase in diuretic activity and a decrease in both acidity and enzyme inhibition with no striking change in lipid solubility An appropriate substituent in position 6 is critical for diuretic activity and produces a decrease in enzyme inhibition. In the thiazide series, 3-substitution increases enzyme inhibition and lipid solubility with little or no change in diuretic potency. Benzthiazide, however, shows a parallel increase in all 3 parameters. In the hydrothiazide series, 3-substitution does not consistently influence the inherently low order of enzyme inhibition but does show a direct relation between diuretic potency and lipid solubility

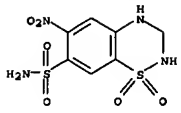
IT 23141-81-3 23141-88-0
RL: BIOL (Biological study)
(as diuretic)

RN 23141-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 23141-88-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1968:95867 CAPLUS
DOCUMENT NUMBER: 68:95867
TITLE: 6-Azido-1,2,4-benzothiadiazines
PATENT ASSIGNEE(S): Farbwerke Hoechst A.-G.
SOURCE: Fr., 4 pp.
CODEN: FRXXAK
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1476505		19670414	FR	
PRIORITY APPLN. INFO.:			DE	19610128

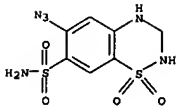
GI For diagram(s), see printed CA Issue.

AB Compds. of the general formula I, useful as diuretic and saluretic agents, are prepared by cyclization of 5-azido-2,4-disulfamoylanilines (II) with aldehydes RCHO. Heating a mixture of 286 g. 5,2,4-Cl(H2NSO2)2C6H2NH2, 200 ml. 80% N2H4.H2O, and 600 ml. HOCH2CH2OMe 5 hrs. under reflux, pouring into 6 l. H2O, and adjusting to pH 7 with HCl gave 254 g. yellow 5-H2NNH-2,4-(H2NSO2)2C6H2NH2 (III), decomposed 215° (aqueous MeOH). A warm solution of 141 g. III in 500 ml. N HCl and 2 l. H2O at 0° was slowly added to 1 l. aqueous 0.5M NaNO2 when II separated and the mixture kept 6 min. at room temperature to give 126 g. II, decomposed 202° (EtOH-C). Refluxing a mixture of 29.3 g. II, 300 ml. EtOH, 20 ml. N NaOH, and 12 ml. 30% aqueous CH2O 1 hr., adding 30 ml. N HCl, filtering, adding 500 ml. H2O to the filtrate, concentrating, and allowing to crystallize gave 16.1 g. I (R = H) (IV), decomposed 200° (20% aqueous EtOH-C). Alternatively, refluxing a mixture of 29.3 g. II, 300 ml. EtOH, 300 ml. 5N HCl, and 3.3 g. paraformaldehyde (or 3.3 g. trioxymethylene) 1 hr. gave a similar yield of IV. By a similar method using different aldehydes were prepared the following I (R, decomposition point, % yield, and recrystg. solvent given): Et, 210°, 83, aqueous Me2NCHO; Me2CHCH2, 192°, 66, 50% aqueous EtOH; MeCH2CH2CHMe, 188°, 56, aqueous EtOH; cyclopentylmethyl, 190°, 53, aqueous EtOH; cyclohexylmethyl, 186°, 59, aqueous EtOH; p-ClC6H4, 208°, 87, EtOH; PhCH2, 194°, 68, -; ClCH2, 183°, 79, --.

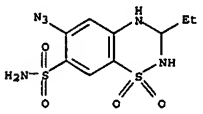
IT 17984-56-4P 17984-57-5P 17984-58-6P
17984-59-7P 17984-60-0P 17984-61-1P
17984-62-2P 17984-63-3P 17984-64-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 17984-56-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

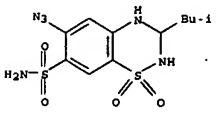
L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



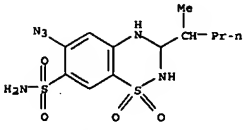
RN 17984-57-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-ethyl-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 17984-58-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-isobutyl-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

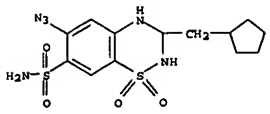


RN 17984-59-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(1-methylbutyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

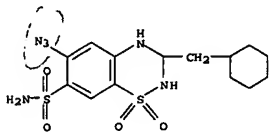


RN 17984-60-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclopentylmethyl)-3,4-

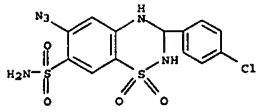
L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 17984-61-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclohexylmethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

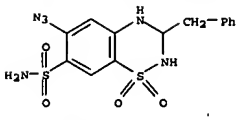


RN 17984-62-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(p-chlorophenyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

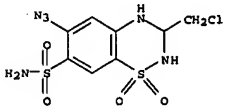


RN 17984-63-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(phenylmethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 17984-64-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(chloromethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



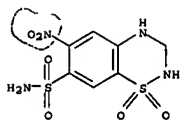
L4 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1967:37968 CAPLUS
DOCUMENT NUMBER: 66:37968
TITLE: 6-Nitro-2-substituted-benzothiadiazines
INVENTOR(S): Robertson, Jerry Earl; Di Pierro, Frank; Biel, John H.
PATENT ASSIGNEE(S): Colgate-Palmolive Co.
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3287215		19661122	US 1961-117288	19600614

GI For diagram(s), see printed CA Issue.
AB Title compds. (I) effective as diuretics and hypotensive agents were prepared by condensation of 2-substituted-2,4-disulfamoyl-5-nitroanilines (II) with aldehydes or acetals. II were prepared by reaction of 5-nitro-aniline-2,4-disulfonyl chloride (III) with 2 equivs. of NH3 followed by an excess of a primary amine. Thus, to 8.5 g. III in 50 ml. EtOH was added 39 ml. 1.27 N alc. NH3. After 30 min., 6 g. MeNH2 in 50 ml. EtOH was added and the reaction mixture held 1 hr. at 30-5°. Dilution with 500 ml. H2O, concentration in vacuo to 400 ml., and cooling gave 4.0 g. 2-methyl-substituted II (IV). Similarly, 8.5 g. III with other amines gave II (g. amine, % yield, and m.p. of II given): 8.1 EtNH2, 75, 168-71° (V); 5.9 PrNH2, 71, 148-53°; 10 benzylamine, 75, 159-61° (VI); 13.5 CF3CH2NH2.HCl, 32 199-201° (VII). A mixture of 4.1 g. IV, 1.9 g. 3-oxobutyraldehyde dimethylacetal (XI) and 1 ml. concentrated HCl in 25 ml. HCONMe2 was held at 30 min. 90-100°. The solvent was removed in vacuo and the residue dissolved in hot EtOH. After filtration, hot water was added to the cloud point and the solution cooled to obtain 3.5 g. I (R1 = Me, R2 = βoxopropyl), m. 215-17°. Other I were prepared similarly (II, aldehyde or acetal, R1, R2, % yield, and m.p. of I, given:) IV (4.1 g.), phenylacetaldehyde dimethylacetal (VIII) (2.3 g.), Me, benzyl, 76, 240-5°; V (4.2), VIII (2.3), Et, benzyl, 74, 207-12°; IV (10.0), dichloroacetaldehyde (IX) (3.7), Me, CHCl2, 32, 266-7° (decomposition); V (3.0), chloroacetal (X) (1.45), Et, CH2Cl, 60, 217-18°; VII (3.8), VIII (1.7), CF3CH2, benzyl, 70, 224-6°; VII (3.8), IX (1.4), CF3CH2, CHCl2, 61, 236-8°; VII (3.0), X (1.4), CF3CH2, CH2CL, 71, 218-20°; VII (3.0), XI (1.5), CF3CH2, AcCH2, 40, 191-5°; V (2.0), XI (1.1), Et, AcCH2, 50, 196-9°; V (1.3), IX (0.6), Et, CHCl2, 24, 222-4°; VI (2.6), IX, benzyl, CHCl2, 28, 222-3°; V (4.5), 3-oxo-3-phenyl-propanal, Et, BzCH2, 14, 221-2°.
IT 23141-88-0DP, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide, 2-substituted derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 23141-88-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

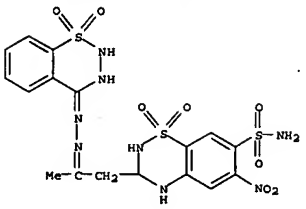


L4 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1966:84632 CAPLUS
DOCUMENT NUMBER: 64:84632
ORIGINAL REFERENCE NO.: 64:15902b-d
TITLE: Substituted 3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides
INVENTOR(S): Robertson, Jerry E.; Biel, John H.
PATENT ASSIGNEE(S): Colgate-Palmolive Co.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3243343		19660329	US 1961-124381	19610717

GI For diagram(s), see printed CA Issue.
AB Imino derivs. of the subject compds. having a carbonyl group were described. E.g., a mixture of 3,4-dihydro-2-methyl-3-acetonyl-7-sulfamoyl-6-trifluoromethyl-1,2,4-benzothiadiazine 1,1-dioxide (8.0 g.), 2.9 g. 1-hydrazinophthalazine, 150 ml. EtOH, and 2 drops AcOH was refluxed 18 hrs., and the solid which separated on cooling, was collected to give Ia. The I prepared were as follows (R, X, R1, Y, m.p., and % yield): H, CF3, Me, Y1 (Ia), 180-2°, 36; H, CF3, Me, Y2, 148-51°, 74; H, CF3, Me, OH, 213-15°, 89; Me, Cl, Me, Y1, 159-61°, 40; H, NO2, H, Y2, amorphous, 80; H, Cl, H, Y1, 172-4°, 40. I have hypotensive and diuretic activity.
IT 5611-04-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-acetonyl-3,4-dihydro-6-nitro-, 1,1-dioxide, 2H-1,2,3-benzothiadiazin-4-ylhydrazone S,S-dioxide
(preparation of)
RN 5611-04-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-acetonyl-3,4-dihydro-6-nitro-, 1,1-dioxide, 2H-1,2,3-benzothiadiazin-4-ylhydrazone S,S-dioxide (7CI, 8CI)
(CA INDEX NAME)

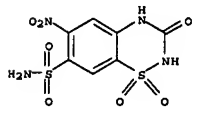
L4 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:457560 CAPLUS
DOCUMENT NUMBER: 63:57560
ORIGINAL REFERENCE NO.: 63:10538f-h
TITLE: . Evaluation of certain hypotensive agents. VII. Tetramethylpiperidine and benzothiadiazinate derivatives
AUTHOR(S): Severs, Walter B.; Kinnard, William J.; Buckley, Joseph P.
CORPORATE SOURCE: Univ. of Pittsburgh, Pittsburgh, PA
SOURCE: Journal of Pharmaceutical Sciences (1965), 54(7), 1025-9
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hypotensive activities of 1-benzyl-3-hydrazinopiperidine dimaleate; 2,2,7,7-tetramethyl-1,4-diazacycloheptan-5-one-HCl; 2,2,6,6,-tetramethyl-4-piperidone oxime; 1-(2,2,6,6-tetramethyl-4-piperidyl)-3-(4-pyridyl)-5-pyrazolone; 3-benzyl-3,4-dihydro-6-nitro-7-sulfamoyl-2H-1,2,4-benzothiadiazine 1,1-dioxide; 2,2,6,6-tetramethylpiperidine 3,4-dihydro-6-nitro-7-sulfamoyl-1,1,3-trioxo-2H-1,2,4-benzothiadiazinate (I),2,2,6,6-tetramethyl-4-piperidone 1,1-dioxo-2H-1,2,3-benzothiadiazin-4-ylhydrazone acetate; and 1-hydrazinophthalazine 3,4-dihydro-6-nitro-7-sulfamoyl-1,1,3-trioxo-2H-1,2,4-benzothiadiazinate (II) were tested in anesthetized dogs and rats: the latter was most sensitive. The compds. acted by ganglionic blockade. I and II caused hypotension in cats. Pre- and postganglionic conduction along sympathetic nerves was depressed but pressor effects to exogenous epinephrine were potentiated.
IT 4040-16-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide, compound with 1-hydrazinophthalazine (1:1) 4086-66-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-benzyl-3,4-dihydro-6-nitro-, 1,1-dioxide 5489-75-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide, compound with 2,2,6,6-tetramethylpiperidine (1:1)
(blood pressure response to)
RN 4040-16-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide, compd. with 1-hydrazinophthalazine (1:1) (7CI, 8CI) (CA INDEX NAME)

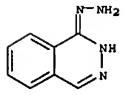
CM 1

CRN 47068-12-2
CMF C7 H6 N4 O7 S2

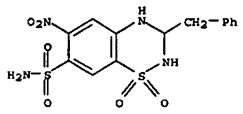


L4 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CM 2

CRN 86-54-4
CMF C8 H8 N4



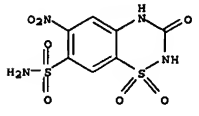
RN 4086-66-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-benzyl-3,4-dihydro-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 5489-75-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide, compd. with 2,2,6,6-tetramethylpiperidine (1:1) (7CI, 8CI) (CA INDEX NAME)

CM 1

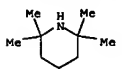
CRN 47068-12-2
CMF C7 H6 N4 O7 S2



CM 2

CRN 768-66-1
CMF C9 H19 N

L4 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

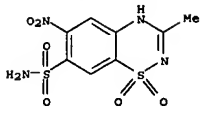


L4 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:454729 CAPLUS
DOCUMENT NUMBER: 63:54729
ORIGINAL REFERENCE NO.: 63:9970f-h,9971a
TITLE: 1,2,4-Benzothiadiazine 1,1-dioxides
INVENTOR(S): Klose, Josef; Starke, Hans
PATENT ASSIGNEE(S): Hans Starke
SOURCE: 4pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DD 33143		19641205	DD	19620309

GI For diagram(s), see printed CA Issue.
AB The reaction of o-aminobenzenesulfonamides with carboxylic acids in the presence of an inorg. acid chloride and a dehydrating agent such as H_2SO_4 produced the title compds. I. Thus, 6 g. of 5-chloro-2,4-di-sulfonamidoaniline was ground with 2 ml. glacial AcOH, 8 ml. $POCl_3$ added, and the mixture heated at 60-70°. With evolution of HCl, the temperature rose to 100-10°, the mixture was cooled to 50-60°, 30 ml. concentrated H_2SO_4 added, and the mixture heated 2-3 hrs. at 60-80°, poured into ice H_2O, and the precipitate washed with H_2O, and recrystd. (80% MeOH) to yield I (R = Cl; R1 = Me), m. 335-7°. The following derivs. of I were also prepared by a similar procedure (R, R1, and m.p. given): Cl, Et, 305-7°; Cl, Pr, 298-300°; Cl, isobutyl, 284-6°, Cl, CH_2Cl, 304-6°; Cl, $CHCl_2$, 310-12°; Cl, CCl_3; 310-15°; Cl, CH_2Br, 296-8°; Cl, $CHBr_2$, 320-2°; Cl, CHBrMe, 288-90°; Cl, CHBrEt, 242°; Cl, CH_2CH_2Ac, 256-8°; Cl, Ph, 354-6°; Cl, p-methoxybenzene, 348-50°; Cl, p-tolyl, 357-8°; Cl, benzyl, 284-6°; Cl, 2,3,4-trimethoxybenzene, 312°; Cl, 4-pyridyl, 375-7°; Cl, 2-pyridyl, 338-40°; Cl, 3-pyridyl, 354-6°; CF_3, Me, 337-9°; CF_3, Et, 338-40°; F, Me, 345-7°; F, Et, 342-4; OMe, Me, 320-2°; F, benzyl, 294-6°; OMe, Et, 315-17°; Me, Me, 352-4°; NO_2, Me, 344-6°.
IT 2850-46-6, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide
(preparation of)
RN 2850-46-6 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

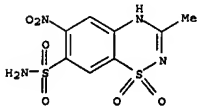


L4 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:91022 CAPLUS
DOCUMENT NUMBER: 62:91022
ORIGINAL REFERENCE NO.: 62:16274g-h,16275a-c
TITLE: 1,2,4-Benzothiadiazine 1,1-dioxides
INVENTOR(S): Novello, Frederick C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

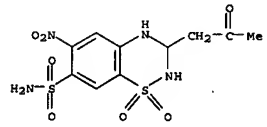
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1111200		19610720	DE	
PRIORITY APPLN. INFO.:			US	19560502

AB The title compds. and alkali salts thereof were prepared by acylation of aminobenzenedisulfonyl chlorides with suitable organic acid chlorides or anhydrides, and treatment of the obtained N-acylaminobenzenedisulfonyl chlorides with NH_3. The compds. may be therapeutically useful as diuretics. Thus, 5 g. 5-chloroaniline-2,4-disulfonyl chloride (I) (m. 130-2°) in 15 cc. Ac_2O kept 45 min. at room temperature, the mixture cooled, filtered, treated with 50 cc. 10% alc. NH_3, evaporated to dryness on the steam bath, the residue heated 2 hrs. at 200°, cooled, and the product recrystd. from dilute alc. gave 90% 6-chloro-3-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, colorless needles, m. 332-3° (decomposition). Similarly prepared were the following 1,2,4-benzothiadiazine 1,1-dioxides: using aniline-2,3-disulfonyl chloride, 50% 3-methyl-7-sulfamoyl-, m. 323-5°; using 4-chloroaniline-2,5-disulfonyl chloride, 43% 7-chloro-3-methyl-6-sulfamoyl-, m. 323-5°; using 5-methoxyaniline-2,4-disulfonyl chloride, 46% 6-methoxy-3-methyl-7-sulfamoyl-, m. 318-20°; using 5-methylaniline-2,4-disulfonyl chloride, 52% 3,6-dimethyl-7-sulfamoyl-, m. 349-51°; and using 5-nitroaniline-2,4-disulfonyl chloride, 49% 3-methyl-6-nitro-7-sulfamoyl-, m. 340-3°. I (6.6 g.) in 10 cc. BzCl kept 17 hrs. at room temperature, and the product filtered, washed with C_6H_6, and recrystd. from C_6H_6 and hexane gave 90% N-benzoyl-5-chloroaniline-2,4-disulfonyl chloride (II), colorless needles, m. 171-3° (decomposition). II (7.4 g.) added to 50-75 cc. liquid NH_3, the mixture evaporated to dryness at room temperature, the residue of N-benzoyl-5-chloro-2,4-disulfamoylaniline, m. 266° (decomposition), heated 2 hrs. at 200°, cooled, dissolved in 50 cc. 5% aqueous NaOH, filtered, the filtrate acidified, and the product filtered, washed with H_2O, and recrystd. from $HCONMe_2$ and H_2O gave 52% 6-chloro-3-phenyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, colorless flakes, m. above 350°. I (5.4 g.) treated 1 hr. with 10 cc. $(PrCO)_2O$ and 10 cc. C_6H_6 as in the preparation of II gave 85% N-butyryl-5-chloroaniline-2,4-disulfonyl chloride (III), colorless needles, m. 121-2°. III (9.9 g.) added to 100 cc. liquid NH_3, the mixture evaporated to dryness at room temperature, the residue dissolved in H_2O, the solution acidified with dilute HCl, and the precipitate filtered and recrystd. from dilute alc. gave 25% 6-chloro-3-propyl-7-sulfamoyl-1,2,4-benzothiadiazine

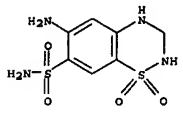
L4 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
1,1-dioxide, colorless needles, m. 302.5-3.5°. Similarly prepd. were the following 1,2,4-benzothiadiazine 1,1-dioxides: using N-caproyl-5-chloroaniline-2,4-disulfonyl chloride, m. 91-3°, 50% 6-chloro-3-amylsulfamoyl-, colorless plates, m. 269-70°; and using N-phenyl-acetyl-5-fluoroaniline-2,4-disulfonyl chloride, m. 195-7°, 23% 6-fluoro-3-benzyl-7-sulfamoyl-, m. 293-5° Cf. CA 62, 10377g.
IT 2850-46-6, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide
(preparation of)
RN 2850-46-6 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



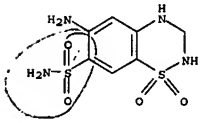
L4 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:29711 CAPLUS
DOCUMENT NUMBER: 62:29711
ORIGINAL REFERENCE NO.: 62:5280c-e
TITLE: Diuretics. 6-Substituted 3-oxoalkyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxides and related anils, oximes, and hydrazones
AUTHOR(S): Robertson, Jerry E.; Dusterhoft, Donald A.; Mitchell, Thomas F., Jr.
CORPORATE SOURCE: Colgate-Palmolive Co., Milwaukee, WI
SOURCE: Journal of Medicinal Chemistry (1965), 8(1), 90-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB Condensation of appropriate oxo aldehydes with 5-substituted 2,4-disulfamoylanilines under acid catalysis provided a group of 6-substituted 3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxides (I) containing 3-oxoalkyl substituents. When β-oxo aldehydes were used and the 2-sulfamoyl group was at least monosubstituted, either the usual ring-closure products or isomeric enol-anils were isolated depending on reaction conditions. Evidence for the enol-anil structures included interconversions between isomeric pairs and spectral and degradative studies. Unusual hydrazones and oximes were prepared and studied. Pharmacol. evaluation revealed several potent diuretic agents and other, less anticipated, biol. properties for the compds. reported.
IT 3754-08-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-acetonyl-3,4-dihydro-6-nitro-, 1,1-dioxide
(preparation of)
RN 3754-08-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-acetonyl-3,4-dihydro-6-nitro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:19027 CAPLUS
DOCUMENT NUMBER: 60:19027
ORIGINAL REFERENCE NO.: 60:3392c-e
TITLE: Antisaluretic thiazide derivatives
AUTHOR(S): Issekutz, Bela, Sr.; Jobbagyi, Nadine; Kelemen, Ester; Oszvald, Edit
CORPORATE SOURCE: Med. Univ., Budapest
SOURCE: Acta Physiologica Academiae Scientiarum Hungaricae (1963), 23(4), 407-13
CODEN: APACAB; ISSN: 0001-6756
DOCUMENT TYPE: Journal
LANGUAGE: German
GI For diagram(s), see printed CA Issue.
AB The antisaluretic effect of 11 thiazide derivs. [I, R = NMe2, NBu2, or piperidino; II, R1 = Cl and R2 = H, CH2Ph, C2H4NMe2(IIa), or CH2CH:CMe2, R1 = H and R2 = NH2 [(IIb); III, R3 = H or Cl; and IV] which were inactive or scarcely active as diuretic agents, was tested. IIa and IIb manifested a poor activity; conversely a high antisaluretic action was found for IV when administered at 0.5-2 mg./kg. to rats. In analogy with aldosterone, IV decreased the Na/K ratio; this effect disappeared in adrenalectomized rats, suggesting that aldosterone is necessary for the activity of IV. To establish if vasopressin (V) is necessary for activity of IV, mannitol was administered to rats treated with IV in order to inhibit the action of IV. Mannitol prevented the antisaluretic effect of IV. Finally, no synergism was observed between IV and V.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(electrolytes in urine after administration)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1964:19026 CAPLUS
DOCUMENT NUMBER: 60:19026
ORIGINAL REFERENCE NO.: 60:3392b-c
TITLE: On the successive stages of the sympatholytic activity of yohimbic acid
AUTHOR(S): Raymond-Hamet
SOURCE: Compt. Rend. (1963), 257(16), 2351-4
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Yohimbic acid has a sympatholytic effect greater than yohimbine, and is less toxic. The sympatholytic action evaluated by the modification of the changes in renal volume and carotid pressure induced by adrenaline, shows the same successive stages as yohimbine. The physiol. effects in the anesthetized dog are detailed.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(electrolytes in urine after administration)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)

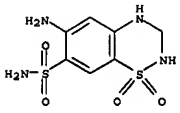


L4 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:417883 CAPLUS
DOCUMENT NUMBER: 59:17883
ORIGINAL REFERENCE NO.: 59:3239d-e
TITLE: Pharmaceutical research [saluretics]
AUTHOR(S): Issekutz, Bela, Sr.
CORPORATE SOURCE: Orvostudomanyi Egyet., Budapest, Hung.
SOURCE: Magy. Tud. Akad. Biol. Orvosi Tud. Oszt. Koezlemen. (1963), 14, 49-63
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Of the 11 thiazide derivs. of little or no diuretic effect, K 35 (6-amino-7-sulfamoyl-3,4-dyhydro-1,2,4-benzothiadiazine 1,1-dioxide) and K 1273 (2-dimethylaminoethyl-6-chloro-3,4-dihydro- 7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide) had a weak anti-saluretic effect; Szi-1181 (3,3,7,7-dipentamethylene-2H,8H-benzo[1,2-e:5,4-e']bis[1,2,4]thiadiazine 1,1,9,9-tetraoxide) was strongly saluretic. The latter, however, had no effect on adrenalectomized animals and did not accentuate the effects of vasopressin, although its effect could be blocked by mannitol.

IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(effect on electrolyte excretion)

RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide (6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:14924 CAPLUS
DOCUMENT NUMBER: 58:14924
ORIGINAL REFERENCE NO.: 58:2461d-f,2462a
TITLE: Synthesis of 6-azido-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides
INVENTOR(S): Siedel, Walter; Sturm, Karl; Nahm, Helmut
PATENT ASSIGNEE(S): Farbwerke Hoechst A.-G.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

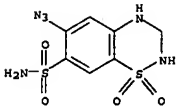
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1135919		19620906	DE 1961-F33088	19610128
FR M1871			FR	
GB 987905			GB	
US 3252862		1966	US	
PRIORITY APPLN. INFO.:			DE	19610128

AB A mixture of 286 g. 5-chloro-2,4-disulfamoylaniline, 200 ml. 80% hydrazine hydrate, and 600 ml. ethylene glycol monomethyl ether is refluxed 5 hrs. The mixture is diluted with 6 l. water, adjusted to pH 7 with HCl, and worked up to give 90% 5-hydrazino-2,4-disulfamoylaniline (I), decomposing at 215°. To a mixture of 500 ml. N HCl and 2 l. water is added 141 g. I with gentle heating. The resulting mixture is cooled to 0° and mixed into 1 l. 0.5M NaNO2 at about 0°. The mixture is stirred 10 min. at room temperature, treated with 500 ml. N HCl, and worked up to give 86% 5-azido-2,4-disulfamoylaniline (II), decomposing at 202°. A mixture of 29.3 g. II, 300 ml. EtOH, 20 ml. N aqueous NaOH, and 12 ml. 30% aqueous CH2O is refluxed 1 hr., treated with 30 ml. N HCl, and worked up to give 52% 6-azido-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (III), decomposing at 200°. III is also prepared using HCl in place of NaOH. Similarly are prepared several substituted III (substituent and decomposition point given): 3-ethyl, 210°; 3-(2-methylpropyl), 192°; 3-(1-methylbutyl), 188°; 3-benzyl, 194°; 3-chloromethyl, 183°; 3-(p-chlorophenyl), 208°; 3-(cyclopentylmethyl), 190°; 3-(cyclohexylmethyl), 186°. These compds. are useful as diuretics.

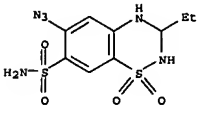
IT 17984-56-4, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-, 1,1-dioxide 17984-57-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-ethyl-3,4-dihydro-, 1,1-dioxide 17984-58-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-isobutyl-, 1,1-dioxide 17984-59-7, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(1-methylbutyl)-, 1,1-dioxide 17984-60-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclopentylmethyl)-3,4-dihydro-, 1,1-dioxide 17984-61-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclohexylmethyl)-3,4-dihydro-, 1,1-dioxide 17984-62-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(p-chlorophenyl)-3,4-

L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
dihydro-, 1,1-dioxide 17984-63-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-benzyl-3,4-dihydro-, 1,1-dioxide 17984-64-4, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(chloromethyl)-3,4-dihydro-, 1,1-dioxide
(prepn. of)

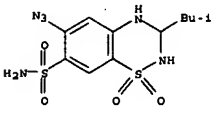
RN 17984-56-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 17984-57-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-ethyl-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

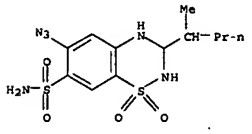


RN 17984-58-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-isobutyl-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

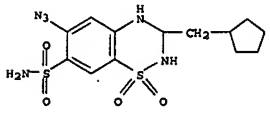


RN 17984-59-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(1-methylbutyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

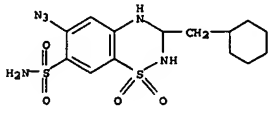
L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



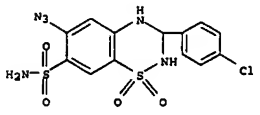
RN 17984-60-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclopentylmethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



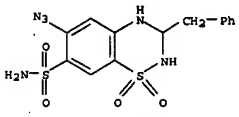
RN 17984-61-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclohexylmethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



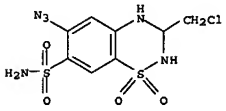
RN 17984-62-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(p-chlorophenyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 17984-63-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(phenylmethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)



RN 17984-64-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(chloromethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

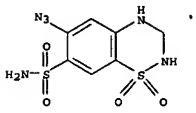


L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:483321 CAPLUS
DOCUMENT NUMBER: 57:83321
ORIGINAL REFERENCE NO.: 57:16639d-g
TITLE: 1,2,4-Benzothiadiazines
PATENT ASSIGNEE(S): Farbwerke Hoechst A.-G.
SOURCE: 15 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

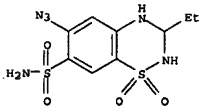
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
BE 613226		19620730	BE	
PRIORITY APPLN. INFO.:			DE	19610128

GI For diagram(s), see printed CA Issue.
AB 3-Alkyl derivs. (I) of 6-azido-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide have diuretic properties and can be used against edemas and idiopathic hypertomia. 5,2,4-H2NNH(H2NO2S)2C6H2NH2 is treated with NaNO2 to form 5,2,4-N3(H2NO2S)2C6H2NH2 (II). II (29.3 g.) is mixed with 300 ml. EtOH, 300 ml. 5N HCl, and 3.3 g. (H2CO)3, the mixture heated to reflux 1 hr., and the mixture kept at room temperature 24 hrs. to give 14.7 g. I (R = H), m. 200° (decomposition) (EtOH-H2O). Similarly prepared are I (R and m.p. given): Et, 210° (decomposition) (HCONMe2-H2O); Me2CHCH2, 192° (decomposition) (50% aqueous EtOH); Me(CH2)2CHMe, 188° (decomposition) (50% aqueous EtOH); cyclopentylmethyl, 190° (decomposition) (aqueous EtOH); cyclohexylmethyl, 186° (decomposition) (50% aqueous EtOH); 4-ClC6H4, 208° (decomposition) (50% EtOH); PhCH2, 194° (decomposition); and ClCH2, 183° (decomposition) (aqueous EtOH).
IT 17984-56-4, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-, 1,1-dioxide 17984-57-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-ethyl-3,4-dihydro-, 1,1-dioxide 17984-58-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-isobutyl-, 1,1-dioxide 17984-59-7, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(1-methylbutyl)-, 1,1-dioxide 17984-60-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclopentylmethyl)-3,4-dihydro-, 1,1-dioxide 17984-61-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclohexylmethyl)-3,4-dihydro-, 1,1-dioxide 17984-62-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(p-chlorophenyl)-3,4-dihydro-, 1,1-dioxide 17984-63-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-benzyl-3,4-dihydro-, 1,1-dioxide 17984-64-4, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(chloromethyl)-3,4-dihydro-, 1,1-dioxide
(preparation of)
RN 17984-56-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-, 1,1-dioxide
(7CI, 8CI) (CA INDEX NAME)

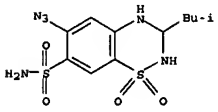
L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



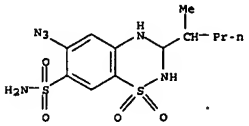
RN 17984-57-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-ethyl-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 17984-58-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-isobutyl-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

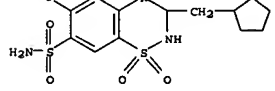


RN 17984-59-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(1-methylbutyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

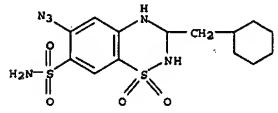


RN 17984-60-0 CAPLUS

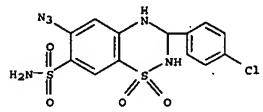
L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclopentylmethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 17984-61-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(cyclohexylmethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

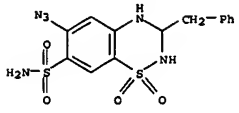


RN 17984-62-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(p-chlorophenyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

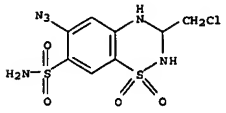


RN 17984-63-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3,4-dihydro-3-(phenylmethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



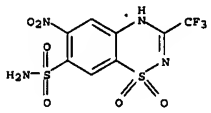
RN 17984-64-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-azido-3-(chloromethyl)-3,4-dihydro-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



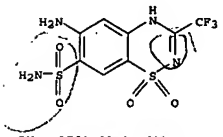
L4 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:469313 CAPLUS
DOCUMENT NUMBER: 57:69313
ORIGINAL REFERENCE NO.: 57:13783d-g
TITLE: 3-Perfluoroalkyl-1,2,4-benzothiadiazine 1,1-dioxide derivatives
PATENT ASSIGNEE(S): Smith Kline & French Laboratories
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 898853		19620614	GB 1960-14234	19600422
US 3261794		1966	US	
PRIORITY APPLN. INFO.:			US	19590501

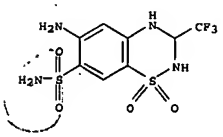
GI For diagram(s), see printed CA Issue.
AB 5-Substituted-2,4-disulfamoylanilines are treated with an excess of RCO2H and anhydride at boiling temps. and the resulting N-acyl derivative cyclized at 200-350° to form I, where R = F3C and R1 = Cl, F3C, NO2, or NH2, and the corresponding 2,3-dihydro compds. by use of NaBH4 or catalytic hydrogenation. The prepared compds. are diuretic, natriuretic and antihypertensive agents. Thus, 18.2 g. 2,4-disulfamoyl-5-chloroaniline (II), 200 ml. F3CCO3H, and 134 g. (F3CCO)2O refluxed overnight, the mixture evaporated, the residue recrystd. from aqueous EtOH gave the NHCOCF3 derivative (III) of II, m. 285°. II (8.3 g.) heated under N at 200°, the temperature raised to 300° in 15 min. and maintained 30 min., cooled, and the residue extracted with boiling EtOH gave I(R = F3C, R1 = Cl),m. above 360°. Similarly, derivs. of I are prepared by alternating the startiug materials and by reduction
IT 798-89-0, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-3-(trifluoromethyl)-, 1,1-dioxide 847-27-8, 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-(trifluoromethyl)-, 1,1-dioxide 3791-98-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-3-(trifluoromethyl)-, 1,1-dioxide
(preparation of)
RN 798-89-0 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-3-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 18 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 847-27-8 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

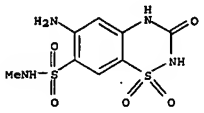


RN 3791-98-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-3-(trifluoromethyl)-, 1,1-dioxide (7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:416929 CAPLUS
DOCUMENT NUMBER: 57:16929
ORIGINAL REFERENCE NO.: 57:3446f-i,3447a-d
TITLE: Synthesis of potential diuretic agents. V. Derivatives of a new tricyclic system, benzo[1,2-e,5,4-e']bis[2-methyl-3,4-dihydro-1,2,4-thiadiazine 1,1-dioxide]
AUTHOR(S): Swett, Leo R.; Freifelder, Morris; Stone, George R.
CORPORATE SOURCE: Abbott Labs., North Chicago
SOURCE: Journal of Organic Chemistry (1961), 26, 3431-4
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 56, 15513c. The title compds, were tested for diuretic activity. A novel synthesis of 4,6-diamino-N1,N3-dimethyl-1,3-benzenedisulfonamide (I) was described. A new tricyclic system was formed by ring closure of I with aldehydes. 4-Amino-6-chloro-1,3-benzenedisulfonamide (236 g.) and 247 g. urea was heated at 610° in a 3 l. glass lined Hastelloy bomb 25 hrs. without shaking. The product was cooled, dissolved in 3 l. H2O, treated with Darco, and filtered. The filtrate was acidified with HCl and left overnight at 4°. The product was filtered, washed with water, and recrystd. from HCONMe2-H2O to give 75% benzo[1,2-e,5,4-e']bis[3-oxo-3,4-dihydro-1,2,4-thiadiazine 1,1-dioxide] monohydrate (II), m. 370° (decomposition). A solution of 25 g. II in 100 ml. HCONMe2 was added dropwise to a stirred suspension of 6.8 g. NaH as 56% oil dispersion in 80 ml. HCONMe2. The mixture was stirred 1 hr., 22.5 g. MeI in 25 ml. HCONMe2 was added dropwise, heated 1 hr., then cooled and diluted with 200 ml. H2O. The precipitate was filtered off and washed with water to give 92% benzo[1,2-e,5,4-e']bis[2-methyl3-oxo-3,4-dihydro-1,2,4-thiadiazine 1,1-dioxide] (III), m. 350-3° (decomposition) (HCONMe2, MeOH and H2O). Ninety grams of III was dissolved in 900 ml. 20% NaOH solution, refluxed overnight, and filtered. The filtrate was cooled and acidified with 6N HCl, and the precipitate thus formed filtered off, washed with H2O, and recrystd. from HCONMe2 to give 70% 4,6-diamino-N1,N3-dimethyl-1,3-benzenedisulfonamide (I), m. 274-6°. Three grams I was dissolved in 150 ml. H2O and 10 ml. HCONMe2, refluxed 15 min. with addition of 8 ml. 37% HCHO solution during this period (a precipitate appeared), further refluxed 30 min., cooled to room temperature, and filtered to give 3.1 g. benzo[1,2-e,5,4-e']bis[2-methyl-3,4-dihydro1,2,4-thiadiazine 1,1-dioxide], m. 318-19° (HCONMe2, MeOH, and H2O). Benzo[1,2-e,5,4-e']bis[3-chloromethyl-2-methyl-3,4-dihydro-1,2,4-thiadiazine 1,1-dioxide] (V), m. 202-3 (HCONMe2-H2O) was prepared from chloroacetaldehyde and I in 79% yield. Benzo[1,2-e,5,4-e']bis[3-carboxy-2-methyl-3,4-dihydro-1,2,4-thiadiazine 1,1-dioxide] (VI), m. 254-6° (decomposition), was obtained from Me dimethoxyacetate and I in 11% yield. These compds. were ineffective diuretic agents. To delineate fully the nature of the reaction of 4-amino-6-chloro-1,2-benzenedisulfonamide and urea the following compds. were prepared 6-Amino-7-(methylsulfamoyl)-3-oxo-3,4-dihydro-1,2,4-

L4 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
benzothiadiazine 1,1dioxide (VII), m. 285-6° (H2O), was prepd. by heating 12.1 g. 6-chloro-2-methyl-3-oxo-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (VIII) and 20.0 g. urea at 180° 24 hrs. The product dissolved in 200 ml. H2O, treated with Darco, filtered, concd. in vacuum, and cooled (cyanuric acid was filtered off), the filtrate acidified with HCl and left at 4° 12 hrs. gave 28% VII. 4-Amino-2-chloro-5-(methylsulfamoyl)benzenesulfonamide (IX) (29.95 g.) and
60.0 g. urea similarly gave VII in 62% yield, m. 283-5°. The mixed m.p. of compd. VII prepd. by the above two procedures was undepressed. The compd. IX m. 196° (25.3%) was isolated by incomplete reaction when VIII and urea were fused, as described above, only for 8 hrs. The m.p. was not depressed when mixed with an authentic sample of IX. This indicated that the reaction of urea with compd. VIII proceeded through the
intermediate IX to give VII. Further chem. evidence was cited in support of structure VII.
IT 92187-68-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-N-methyl-3-oxo-, 1,1-dioxide
(preparation of)
RN 92187-68-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-N-methyl-3-oxo-, 1,1-dioxide (7CI) (CA INDEX NAME)

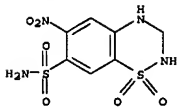


L4 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:410899 CAPLUS
DOCUMENT NUMBER: 57:10899
ORIGINAL REFERENCE NO.: 57:2236a-c
TITLE: 6-Substituted-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides
INVENTOR(S): Hoehn, Hans
PATENT ASSIGNEE(S): Chemische Fabrik von Heyden A.-G.
SOURCE: 3 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

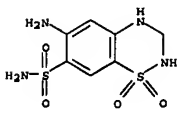
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1118788		19611207	DE 1959-C18459	19590220

AB The title compds., substituted in the 6-position by R = Br, Cl, CF3, NO2, OMe, or a lower alkyl radical, were prepared in a 80-90% yield by treating
2,4-disulfochloro-5-(R-substituted)aniline and hexamethylenetetramine (I) or HCHO and NH3 (molar ratio 3:2) in an organic solvent at room temperature and
heating the product in water or an organic solvent at 50-100° and finally boiling the salts or methylol compds. obtained in water. Thus, 3.2 g. 5-chloroaniline-2,4-di(sulfonyl chloride) (II), m. 142° was dissolved in 20 ml. acetone and at room temperature 3.5 g. I in 10 ml. water
added. After the addition the condensation compound (III) precipitated in 95-7%
yield, m. 191° (decomposition). III was also prepared by adding all at one time a freshly prepared mixture of 7.6 ml. 25% NH4OH and 15 ml. 30% HCHO
to 3.2 g. II in 20 ml. EtOH at room temperature A mixture of 4 g. III and 100 ml.
water was heated to 80° to complete solution After 2 hrs. boiling, the solution was cooled, the precipitate filtered off, and the precipitate boiled in water
till no more HCHO escaped to yield 80-90% (6-R-substituted)-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (IV) (R = Cl), m. 262° Similarly were prepared IV (R, m.p. of condensation product, and m.p. of free compound given): Br, 179-84° (decomposition), 279-80° NO2,151-4° (decomposition), 258-9°; Me, 177-80° (decomposition), 259-61°; OMe, 190-200° (decomposition), 200% CF3, -, 265°.
IT 23141-88-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide
(preparation of)
RN 23141-88-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide
(6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

L4 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



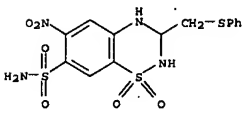
L4 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:56941 CAPLUS
DOCUMENT NUMBER: 56:56941
ORIGINAL REFERENCE NO.: 56:10861c-e
TITLE: Diuretic effects of dihydrochlorothiazide derivatives
AUTHOR(S): Ishekuts, B.
CORPORATE SOURCE: Med. Univ., Budapest
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1961), 24, 557-61
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Chlorothiazide, 6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, yields a 3,4-dihydro derivative, hypothiazide (I). Taking the diuretic and
saluretic activities (in rats) of chlorothiazide as 1, resp. activities of
I were 4.1, 10.8; among derivs., peak activity (16.0, 40.0) was reached with pentamethylene instead of the 2 H atoms in the 3-position. Other activating substitutions were 5-Cl (5.8, 4.0); 3-Me (1.7, 4.0); 3-CCl3 (1.1, 6.2); and ring rupture at 2 to form 1-SO2NH2 and NHCH2OMe groups (3.5, 7.5). Other substitutions, giving activities less than 1, were 6-NH2, 3-H (no activity), 5-Br. After ring rupture the groups SO2NHMe (0.7, 0.9) and SO2NEt2 (0,0) lowered activity. Effective diuretic doses (mg./kg.) were determined for I derivs. in which the 3-CH2 group is replaced:
CHEt 0.5; CHCH:CH2 0.2; CHCH:CHMe 1.0; and side rings, 4-methylcyclohexyl 4.0; cyclopentyl 0.2; thiacyclohexyl 0.2; dithiacyclopentyl 0.1; piperidyl
4.0; N-ethylpiperidyl 4.0; I 0.2. The relatively inactive N-ethylpiperidyl derivative had a pronounced hypotensive effect.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(as diuretic)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:18376 CAPLUS
DOCUMENT NUMBER: 56:18376
ORIGINAL REFERENCE NO.: 56:3496f-h
TITLE: 3-Mercaptoalkyl-3,4-dihydro- 1,2,4-benzothiadiazine 1,1dioxide derivatives
INVENTOR(S): Lund, Frantz; Godtfredsen, Wagn Ole
PATENT ASSIGNEE(S): Loevens Kemiske Fabrik ved. A. Kongsted
SOURCE From: Division of Brit. 863,474.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

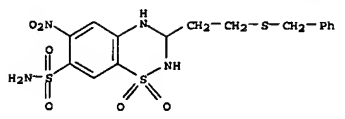
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 863508			GB	19600120

AB CA 55, 19971b. Derivs. of 7-sulfonyl-3,4-dihydro-1,2,4benzothiadiazine 1,1-dioxide (I) were prepared They exert saluretic effects in humans. Thus, 2.9 g. 5-chloro-2,4-disulfa-moyaniline and g. phenylthioacetaldehyde diethyl acetal was refluxed 5 hrs. in 75 ml. dioxane with a catalytic amount of toluenesulfonic acid, the mixture evaporated to dryness, the residue triturated with CH2Cl2, then hexane, the precipitate dissolved in EtOAc, precipitated by adding CH2Cl2-hexane, then precipitated from EtOH-H2O to give 3-phenylthiomethyl-6-chloro derivative of I, m. 201°. Similarly prepared were 3-benzylthiomethyl-6chloro derivative of I, m. 213°; 3-phenylthiomethyl-6-nitro derivative of I, m. 227.5°; 3-(β-benzylthioethyl)-6-nitro derivative of I, m. 189°; 3-phenylthiomethyl-6-methyl derivative of I, m. 202°; 3-benzylthiomethyl-6-methyl derivative of I, m. 203-4°.
IT 93867-61-9, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-[(phenylthio)methyl]-, 1,1-dioxide
94672-48-7, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-[2-(benzylthio)ethyl]-3,4-dihydro-6-nitro-, 1,1-dioxide
(preparation of)
RN 93867-61-9 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-[(phenylthio)methyl]-, 1,1-dioxide (7CI) (CA INDEX NAME)

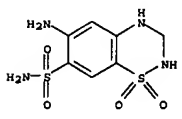


RN 94672-48-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-[2-(benzylthio)ethyl]-3,4-dihydro-6-nitro-, 1,1-dioxide (7CI) (CA INDEX NAME)

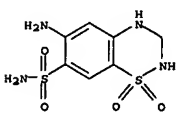
L4 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:10546 CAPLUS
DOCUMENT NUMBER: 56:10546
ORIGINAL REFERENCE NO.: 56:1968a-c
TITLE: Diuretic effect of hydrochlorothiazide derivatives
AUTHOR(S): Issekutz, Bela., Sr.; Jobbagyi, Zsolt; Oszvald, Edit; Szekely, Mihaly
CORPORATE SOURCE: Orvostudomanyi Egyetem, Budapest, Hung.
SOURCE: Magyar Tudomanyos Akad. Biol. es Orvosi Tudomanyok Osztalyanak Kozlemenyei (1961), 12, 61-76
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB As compared with chlorothiazide, the effect of hydrochlorothiazide (I) was 10-fold stronger. Its effect could be increased further by introducing a dichloromethyl group at C-3, or by building a 3rd ring into the compound at this point. The resulting 3,3-pentamethylene-I and 3,3-(3-thiapenta-methylene)-I were 2-4-fold more effective than I. The I derivs. increased Na excretion. As long as a Na excess was present in the organism, the K excretion was not affected. Extirpation of the adrenals did not alter the effect of I if the rats were kept on a physiol. sufficient cortexone and hydrocortisone regimen. Excess cortexone doses >1.5 mg./kg. or >0.1 mg. aldosterone/kg. inhibited the I effect.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(as diuretic)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:10545 CAPLUS
DOCUMENT NUMBER: 56:10545
ORIGINAL REFERENCE NO.: 56:1967g-i,1968a
TITLE: Effect of adrenergic blocking agents on some metabolic actions of catechol amines
AUTHOR(S): Mayer, Steven E.; Moran, Neil C.; Fain, John
CORPORATE SOURCE: Emory Univ., Atlanta, GA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1961), 134, 18-27
CODEN: JPETAB; ISSN: 0022-3565
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Dichloro-isoproterenol (I) is known to prevent both adrenaline (II)-induced increase of contractile force and activation of phosphorylase in the dog heart in situ. The present study demonstrates that I almost completely abolishes the increase in blood sugar and free fatty acids induced by II, noradrenaline (III), and isoproterenol in the dog. The hyperlactic-acidemic effect of II is partly blocked. I does not block II-induced hyperglycemia in mice. In contrast to I, phenoxybenzamine (IV) does not affect the hyperglycemia or increase in blood lactic acid induced by II in the dog. Ergotamine antagonizes the hyperglycemia but not the increase in lactic acid. IV effectively blocks the vasopressor response to II and III, and ergotamine produces maximal reversal of II. None of these drugs in the doses used antagonized the pos. inotropic effect of adrenergic stimuli. Both I and IV increase blood glucose and lactic acid. High doses of I appear to antagonize the hyperglycemic action of low doses. The hyperglycemia and lactic acid increase produced by IV are antagonized by I. I also produces a marked and sustained increase in free fatty acids even with doses which do not block the action of II. Possible mechanisms of action are discussed.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(as diuretic)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)

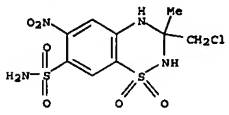


L4 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:105988 CAPLUS
DOCUMENT NUMBER: 55:105988
ORIGINAL REFERENCE NO.: 55:19971b-g
TITLE: Benzothiadiazine derivatives
INVENTOR(S): Lund, Frantz; Godtfredsen, Wagn O.
PATENT ASSIGNEE(S): Lovens Kemiske Fabrik ved. A. Kongsted
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

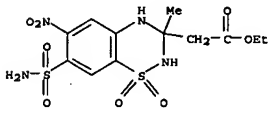
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 863474		19610322	GB	
DE 1226107			DE	
DK 97587			DK	
US 3254076		1966	US	
US 3254077		1966	US	

AB 6-Substituted 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I), prepared from a substituted 2,4-disulfamoylaniline (II) and RCHO, H2C(OMe)2, or H2C:CHOR, had saluretic effects in rats and humans. Thus, a solution of 3.2 g. 5-trifluoromethyl-2,4-disulfamoylaniline, 25 ml. EtOH, and 10 ml. ethylal, and a catalytic amount of p-MeC6H4SO3H was refluxed overnight and worked up to give the 6-trifluoromethyl derivative of I, m. 271-2°. By varying RCHO (or acetal) reactant, the following 3-substituted-6-trifluoromethyl analogs of I were prepared: Me (from EtOCH: CH2, EtOCHClMe, or ClCH2CHO), m. 240-40.5°; ClCH2, m. 245-45.5;° BrCH2 (III), m. 209-10°; Et, m. 255-6°; Pr, 232-3°; iso-Pr, m. 244-5°; Bu, m.216-17°; δ-hydroxybutyl, m. 175-5.5°; n-pentyl, m. 190-1°; γ-nitropentyl, m. 243.5-5°; acetonyl, m. 208-9°; β-methoxyethyl, m. 188-90°; dicarbethoxymethyl, m. 232-4°; Ph, m. 218-19.5°; Ph2CH, m. 261-2.5°; p-methoxyphenethyl, m. 250-1.5°; benzyl (IV), m. 224-5°; phenethyl, m. 235-6°; α-phenylethyl (V), m. 243-4°; p-chlorobenzyl, 243-4°; benzyloxymethyl, m. 221-21.5°; phenoxymethyl, m. 244-6°; p-nitrophenoxymethyl, m. 261-2° (decomposition); p-aminophenoxymethyl, m. 193-4°; 2,4-dichlorophenoxymethyl, m. 230-1°; Bz, 261-2°; benzylthiomethyl, 202-3°; β-benzylthioethyl, 134-46°; 2-pyridyl, m. 304-6° (decomposition); 2-furyl, m. 190-2°; 3-cyclohexyl, m. 258-9°; 1-propenyl, m. 213-5°; n-hexyl, 178-9°; 3-pyridyl, m. 240-1°; styryl, m. 167-9°. Substitution of a ketone for the aldehyde reactant yields the corresponding 3,3-disubstituted-6-trifluoromethyl analog of I; thus, acetone and 6-trifluoromethyl derivative of II gave the 3,3-dimethyl-6-trifluoromethyl derivative of I. The following were prepared similarly: 3-methyl-3-ethyl, m. 212-13°; 3-methyl-3-chloro (VI), m. 227-7.5°; 3-methyl-3-carbethoxy, m. 191-4°; 3-methyl-3-carbethoxymethyl, m. 150-2°; cyclopentane-1,3-spiro, m. 232-4°; cyclohexane-1,3-spiro, m. 261-2°; 2-chlorocyclohexane-1,3-spiro, m. 218-19°; 4-chlorocyclohexane-1,3-

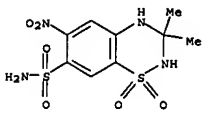
L4 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
spiro (VII), m. 217-18°. By varying the 5-substituent in II, the following 3,3-dimethyl-6-substituted-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides were prepd.: NO2, m. 233-3.5°; Cl (VIII), m. 230-1°; Br, m. 228-9°; MeO, m. 240-0.5°; Me, m. 243-4°; H, m. 242-2.5°. The following were prepd. similarly (substituents given): 3-Me, 3-Et, 6-Cl, m. 231-3°; 3-Me, 3-ClCH2, 6-NO2; 3-Me, 3-CO2Me, 6-NO2, m. 218-19°; cyclopentane-1,3-spiro-6-chloro, m. 234°; cyclohexane-1,3-spiro-6-bromo (IX), m. 281-3°; 2-methylcyclohexane-1,3-spiro-6-bromo, m. 231-3°; 2-chlorocyclohexane-1,3-spiro-6-chloro, m. 223-5°; 3-methyl-3-acetyl-6-chloro, m. 246-7°. Tests on groups of ten persons indicated that 2.0 mg. IV had the same saluretic effect as 20 mg. of the 6-Cl deriv. of I. III-IX were potent saluretic agents in rates.
IT 100255-92-3, 2H-1,2,4-Benzothiadiazine-3-acetic acid, 3,4-dihydro-3-methyl-6-nitro-7-sulfamoyl-, ethyl ester, 1,1-dioxide 100704-66-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3,3-dimethyl-6-nitro-, 1,1-dioxide 101167-06-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(chloromethyl)-3,4-dihydro-3-methyl-6-nitro-, 1,1-dioxide
(preparation of)
RN 100255-92-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-3-acetic acid, 3,4-dihydro-3-methyl-6-nitro-7-sulfamoyl-, ethyl ester, 1,1-dioxide (6CI) (CA INDEX NAME)

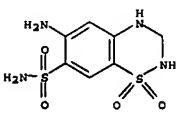


RN 100704-66-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3,3-dimethyl-6-nitro-, 1,1-dioxide (6CI) (CA INDEX NAME)



RN 101167-06-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(chloromethyl)-3,4-dihydro-3-methyl-6-nitro-, 1,1-dioxide (6CI) (CA INDEX NAME)

L4 ANSWER 26 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:66336 CAPLUS
DOCUMENT NUMBER: 55:66336
ORIGINAL REFERENCE NO.: 55:12643c-e
TITLE: Relation between saluretic activity and carbonic anhydrase-inhibiting effects of aromatic sulfonamides
AUTHOR(S): Kobinger, W.; Katic, Ulla; Lund, F. J.
CORPORATE SOURCE: Leo Pharm. Products Copenhagen, Den.
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1961), 240, 469-82
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The saluretic activity in rats and the carbonic anhydrase (I)-inhibitory activity in vitro was compared in several aromatic sulfamoyl compds. with free and alkylated sulfamoyl groups. Saluretic active disulfamoylanilines showed a higher degree of I-inhibitory activity than saluretic-inactive analogs. No such correlation was observed in dihydrobenzothiadiazines. There was, however, some correlation between the saluretic activity of dihydrobenzothiadiazines and the saluretic and I-inhibitory activities in vitro of their corresponding disulfamoylanilines, which can be formed by hydrolysis of the former. In compds. where the sulfamoyl groups are N-alkylated, no in vitro I inhibition can be expected. After peroral administration of saluretic-active N-alkylated compds., I-inhibitory activity was found in the urine, so that dealkylation can be assumed. I inhibition seems to be one of the conditions for saluretic activity.
IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(carbonic anhydrase inhibition by, diuresis and)
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)

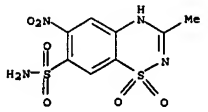


L4 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:48769 CAPLUS
DOCUMENT NUMBER: 55:48769
ORIGINAL REFERENCE NO.: 55:9440f-i,9441a
TITLE: Nitroanilinedisulfonyl chlorides
INVENTOR(S): Novello, Frederick C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: Continuation-in-part of U.S. 2,910,474 (CA 54, 4636e)
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

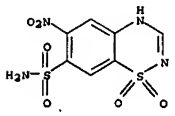
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2961463		19601122	US 1957-683705	19570913

AB The title compds. are prepared by chlorosulfonation of a nitroaniline in the presence of an alkali metal halide. Thus, 64 g. m-nitroaniline is added dropwise with stirring to 375 ml. ClSO3H, the mixture cooled in an ice bath, 350 g. NaCl added in portions over 1-2 hrs., the mixture heated gradually to 150°, after 3 hrs. at 150-60°, the mixture cooled in an ice bath, treated with 1 l. cold H2O, extracted with Et2O, the extract washed with H2O, dried (Na2SO4), and the Et2O evaporated to yield 5-nitroaniline-2,4-disulfonyl chloride (I). In like manner, N-methyl-3-nitroaniline, N-ethyl-3-nitroaniline, and N,N-diethyl-m-nitroaniline with ClSO3H yield the corresponding 2,4-disulfonyl chlorides. Also, Na 5-amino-2-nitrobenzenesulfonate is treated with ClSO3H to produce 4-nitroaniline-2,5-disulfonyl chloride. I (5 g.) in 15 ml. Ac2O is allowed to stand at room temperature 45 min. to yield 5-nitroacetanilide-2,4-disulfonyl chloride (II). In like manner, Ac2O is replaced with butyric anhydride, n-caproic anhydride, BzCl, PhCH2COCl, and lauroyl chloride to yield the corresponding derivs. Also, N-methyl-5-nitroaniline-2,4-disulfonyl chloride is treated with Ac2O or BzCl to yield N-methyl-5-nitroacetanilide-2,4-disulfonyl chloride or N-benzoyl-N-methyl-5-nitroaniline-2,4-disulfonyl chloride, resp. Any of the title compds. can be converted to the corresponding disulfamoyl derivative by the following procedure. I is cooled and treated with 28% NH4OH 1 hr. on a steam bath, cooled, filtered, the solid washed with H2O, dried, and crystallized from dilute EtOH to yield 2,4-disulfamoyl-5-nitroaniline (III), needles, m. 260-2°. Any of the disulfamoylnitroanilines can be converted to the nitrobenzothiadiazine 1,1-dioxide (IV) derivative as follows. III (5 g.) in 175 ml. 98-100% HCO2H is refluxed 3 hrs., cooled, the crystals filtered off, and washed with EtOH to yield 6-nitro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 338-9° (decomposition). Also, the title compds. can be converted directly to IV as follows. II is treated with 50 ml. 10% alc. NH4OH, the mixture evaporated to dryness, the residue heated at 200° 0.5-1 hr., cooled, and crystallized from dilute

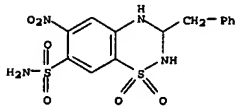
L4 ANSWER 27 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
EtOH to yield 3-methyl-6-nitro-7-sulfamoyl-1,2,4-benzothiazine 1,1-dioxide.
IT 2850-46-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide 23141-81-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide
(preparation of)
RN 2850-46-6 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 23141-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)

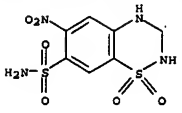


L4 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:39254 CAPLUS
DOCUMENT NUMBER: 55:39254
ORIGINAL REFERENCE NO.: 55:7664d-f
TITLE: Aromatic sulfamoyl compounds with diuretic action
AUTHOR(S): Lund, F. J.; Kobinger, W.
CORPORATE SOURCE: Research Labs. Leo Pharm. Prods., Copenhagen
SOURCE: Acta Pharmacologica et Toxicologica (1960), 16, 297-324
CODEN: APTOA6; ISSN: 0001-6683
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A relation was found between constitution and activity of substituted 2,4-disulfamoylanilines (DSA) and substituted 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (DBT). DSA and DBT compds. showed a distinct relation between substitution in the benzene ring and saluretic activity. Substitution in the heterocyclic ring of DBT compds. yielded some substances considerably more potent than the known hydroflumethiazide (6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide) and hydrochlorothiazide. Of these substances, benzylhydroflumethiazide(Centyl)(the 3-benzyl derivative of hydroflumethiazide), which in human expts. showed the saluretic activity expected on the basis of the animal expts., was selected for further clin. use. Among the active substances studied, no differences in the urinary electrolyte-excretion pattern were detected by the method used.
IT 4086-66-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-benzyl-3,4-dihydro-6-nitro-, 1,1-dioxide 23141-88-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide 100255-92-3, 2H-1,2,4-Benzothiadiazine-3-acetic acid, 3,4-dihydro-3-methyl-6-nitro-7-sulfamoyl-, ethyl ester, 1,1-dioxide 100704-66-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3,3-dimethyl-6-nitro-, 1,1-dioxide
(as diuretic)
RN 4086-66-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-benzyl-3,4-dihydro-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)

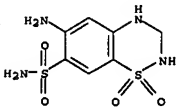


RN 23141-88-0 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide
(6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

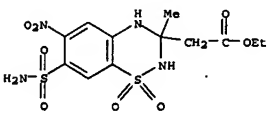
L4 ANSWER 28 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



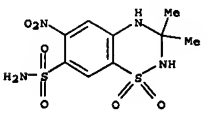
RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



RN 100255-92-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-3-acetic acid, 3,4-dihydro-3-methyl-6-nitro-7-sulfamoyl-, ethyl ester, 1,1-dioxide (6CI) (CA INDEX NAME)



RN 100704-66-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3,3-dimethyl-6-nitro-, 1,1-dioxide (6CI) (CA INDEX NAME)

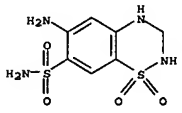


L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:120498 CAPLUS
DOCUMENT NUMBER: 54:120498
ORIGINAL REFERENCE NO.: 54:23066f-i
TITLE: The diuretic action of dihydrochlorothiazide derivatives
AUTHOR(S): Issekutz, B.; Jobbagyi, E.; Szekely, M.
CORPORATE SOURCE: Univ. Budapest
SOURCE: Therap. Hung. (1959), 7, 15-7
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB The following compds. were studied in adult rats: chlorothiazide (K30), 6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (K32), 6-chloro-7-sulfamoyl-3,4-dihydro-3-trichloromethyl-1,2,4-benzothiadiazine 1,1-dioxide (K33), 6-chloro-7-sulfamoyl-3,4-dihydro-3-methyl-1,2,4-benzothiadiazine 1,1-dioxide (K34), 6-amino-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (K35), benzo-1,2,4,9,8,6-dithiadiazine 1,1,9,9-tetroxide (K36), 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (K37), 5,6-dichloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (K38), and 7-sulfamoyl-3-trichloromethyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (K39). K37 and K38 with only a H at C-6 had a weak diuretic action at a dose of 4 mg./kg. A dose of 2 mg. of K30/kg. produced a larger output of Cl than 4 mg./kg. K36 was ineffective over the dose range of 0.54 mg./kg. Cl excretion showed a marked decline with K36. The dihydrochlorothiazide compds. proved to be more potent than K30. With respect to their effect on water diuresis, the order of potency was as follows: K38 > K32 > K34 > K33 > K30; for Cl excretion it was K32 > K34 > K38 > K33 > K30. K38 was most effective for water diuresis while K32 and K34 would be the compds. of choice for increasing the Cl output. The activity of some of these compds. was compared with that of urea. Albuminuria, feebleness, and anorexia were observed in animals given 2-3 g. of K30/kg. All of the test animals survived.

IT 86579-01-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(as diuretic)

RN 86579-01-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-, 1,1-dioxide
(6CI, 7CI, 9CI) (CA INDEX NAME)



L4 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L4 ANSWER 30 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:103487 CAPLUS
DOCUMENT NUMBER: 54:103487
ORIGINAL REFERENCE NO.: 54:19704b-i,19705a-i,19706a-i,19707a-b
TITLE: Diuretics: 1,2,4-benzothiadiazine 1,1-dioxides
AUTHOR(S): Novello, Frederick C.; Bell, Stanley C.; Abrams, Ester
L. A.; Ziegler, Carl; Sprague, James M.
CORPORATE SOURCE: Merck and Co., Inc., West Point, PA
SOURCE: Journal of Organic Chemistry (1960), 25, 970-81
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:103487

AB Ring closure of aniline-2,4-disulfonamides with acylating agents, aldehydes, or CO(NH2)2 to give sulfamoylbenzothiadiazine 1,1-dioxide derivs. was described. Sulfamoylbenzothiadiazine 1,1-dioxides promoted excretion of NaCl in animals and man and constituted a novel class of orally effective diuretic agents. Several aspects of the chemistry of this class of compds. were reported in detail. The following procedure was illustrative of the HCO2H ring closure of aniline-2,4-disulfonamides to benzothiadiazine 1,1-dioxides. The yield was typical. 5-Chloro-2,4-disulfamoylaniline (5.7 g.) in 75 ml. 98-100% HCO2H refluxed 24 hrs., the mixture cooled, 100 ml. H2O added, the product collected, washed, and recrystd. gave 6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (Ia) in 90% yield. 5-Amino-2,4-disulfamoylaniline (1.3 g.) in 20 ml. 98-100% HCO2H refluxed 2.5 hrs. and cooled gave 1.14 g. benzo[1,2-e,5,4-e']bis-1,2,4-thiadiazine 1,1-dioxide, m. above 500° (HCONMe2). 2-Methylsulfamoylaniline (2 g.) and 5 ml. Et orthoformate heated 0.5 hr. at 125-35° in an open flask, concentrated to dryness in vacuo, and the residue recrystd. gave 1.6 g. 2-methyl-1,2,4-benzothiadiazine 1,1-dioxide (I), needles. Recrystn. of I from 50% hot aqueous alc. gave 2-(N-formyl-N-methylsulfamoyl)aniline, m. 116-18°. Ring closure of 5-chloro-2,4-bis(methylsulfamoyl)aniline was similarly carried out to give 6-chloro-2-methyl-7-methylsulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide; recrystn. from hot aqueous alc. gave 5-chloro-2,4-bis(methylsulfamoyl)-N-formylaniline, plates, m. 192-5°. Ia (15 g.) in 100 ml. Et orthoformate (II) refluxed 24 hrs. and cooled gave 15.4 g. 6-chloro-7-ethoxymethylenesulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (III), m. 195-6°, resolidified and m. 210-11° (MeCN-Et2O). 6-Chloro-2-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (IV) and II gave 6-chloro-7-ethoxymethylenesulfamoyl-2-methyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 155-7°. Similarly, 6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide and II gave 6-chloro-7-ethoxymethylenesulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 22-30° (effervescence). NH3 passed into 6.5 g. III in 50 ml. anhydrous alc. 0.5 hr. gave 3.6 g. 7-aminomethylenesulfamoyl-6-chloro-1,2,4-benzothiadiazine 1,1-dioxide, m. 309-11° (alc.). IV similarly treated with NH3 gave 7-aminomethylenesulfamoyl-6-chloro-2-methyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 233-4°. 5-Chloroacetanilide-2,4-disulfonyl chloride (4.4 g.) added por-tionwise to 50 ml. 10% alc.-NH3, the solution evaporated to dryness, and the residue recrystd. from aqueous alc. gave 6-chloro-3-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide. Similarly, with concentrated NH4OH 6-chloro-3-propyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide and 3-amyl-6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide were prepared from the corresponding

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N-acylanilinedisulfonyl chlorides. 5-Chloro-2,4-disulfamoyl-N-(chloroacetyl)aniline (7.2 g.) in 30 ml. HCONMe2 heated 1.5 hrs. with 2.3 g. anhyd. KF, cooled, and dild. with H2O gave 5.5 g. 3-chloromethyl-6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide. Method (A). 5-Chloroaniline-2,4-disulfonyl chloride (7.2 g.) in 13 ml. BzCl left overnight at room temp. gave 10.9 g. 5-chloro-N-benzoylaniline-2,4-disulfonyl chloride, which washed and heated 2 hrs. on the steam bath with C6H6 and 50 ml. concd. NH4OH gave 2.7 g. 6-chloro-3-phenyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (V), needles. Acidification of the ammoniacal filtrate gave 5-chloro-2,4-disulfamoyl-N-benzoylaniline (VI). Method (B). VI (1 g.) in 25 ml. concd. NH4OH left 48 hrs. at room temp. gave 84% V. In like manner, ring closure of 5-chloro-2,4-disulfamoyl-N-(p-chlorobenzoyl)aniline gave 85% 3-(p-chlorophenyl)-6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide. 5-Chloro-2,4-disulfamoyl-N-(o-chlorobenzoyl)aniline similarly afforded 56% 3-(o-chlorophenyl)-6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide. The following substituted 1,2,4-benzothiadiazine 1,1-dioxides were obtained (substituents at 2, 3, 5, 6, and 7, recrystn. solvent, and m.p. given): H, H, H, H, SO2NH2, alc.-H2O, 319-20°; H, H, H, F, SO2NH2, alc.-H2O, 304-5°; H, H, H, Cl, SO2NH2, alc.-H2O, 342.5-3.0°; H, H, H, Br, SO2NH2, HCONMe2-H2O, 347-9°; H, H, H, CF3, SO2NH2, alc.-hexane, 294-5°; H, H, H, Me, SO2NH2, AcOH-H2O, 344-5°; H, H, H, OMe, SO2NH2, alc.-H2O, 305-7°; H, H, H, NO2, SO2NH2, alc.-H2O, 338-9°; H, H, H, NH2, SO2NH2, alc.-H2O, 323-4°; Me, H, H, Cl, SO2NH2, HCONMe2-Et2O, 217-20°; H, Me, H, Cl, SO2NH2, alc., 332°; H, Pr, H, Cl, SO2NH2, alc.-H2O, 305-7°; H, C5H11, H, Cl, SO2NH2, alc.-H2O, 269-70°; H, ClCH2, H, Cl, SO2NH2, alc.-H2O, 323-6°; H, Ph, H, Cl, SO2NH2, HCONMe2-H2O, above 350°; H, o-ClC6H4, H, Cl, SO2NH2, alc.-H2O, above 350°, H, p-ClC6H4, H, Cl, SO2NH2, alc.-H2O, above 350°; H, H, Cl, H, SO2NH2, alc.-H2O, 276.5-7.5°; H, H, Cl, Cl, SO2NH2, alc.-H2O, 355-6°; H, H, I, Cl, SO2NH2, HCONMe2H2O, 276-7°; Me, H, H, Cl, SO2NHMe, alc., 219-21°; p-ClC6H4, H, H, Cl, SO2NHC6H4Cl-p, MeCN, 247-9°; H, H, H, Cl, SO2NMe2, alc.-H2O, 265-7°; H, H, SO2NH2, H, H, Me2CO-C6H6, 249-50°; H, H, SO2NH2, H, Br, Me2CO, 291-2°; H, H, SO2NH2, H, SO2NH2, alc.-H2O, 316-18°; H, H, H, SO2NH2, H, alc.-H2O, 309-12°; H, H, H, SO2NH2, Cl, Me2CO-ligroine, 327-30°; H, H, H, Cl, H, butanone, 253-4°; H, H, H, Cl, Cl, Me2CO-ligroine, 293-4°; H, H, H, Cl, Me, alc.-H2O, 287-8°; H, H, H, Me, Cl, MeCN, 260-1°; H, H, H, Cl, MeSO2, alc.-H2O, 329-31°; Me, H, H, H, H, alc., 95-7°. The general procedure for the prepn. of 3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides.

Method (A). The orthanilamide compd. (0.02 mole) and 0.025 mole of 37% HCHO in 50 ml. 90% alc.-H2O contg. 300 mg. NaOH heated 2 hrs. on the steam bath, acidified, and the mixt. cooled gave 80% yield. Method (B): acid catalyzed ring closure. The orthanilamide compd. (0.02 mole) and 0.04 mole paraformaldehyde in 60 ml. alc. and 60 ml. 6N HCl heated and after 1 hr. the product isolated gave an average yield of 85-90%. The following substituted 3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were thus obtained (substituents at 5 and 6 and m.p. given): H, H, 216-17°; H, Cl, 262-3°; H, Br, 287-8°; H, CF3, 263-4°; H, Me, 253-4°; H, NO2, 263.5-4.5°; Cl, Cl, 288-9°. Likewise the following 6-chloro-substituted 3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides were obtained (substituents at 2, 4, and 7, m.p., and recrystn. solvent given): H, H,

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164-6°, PhMe; H, Me, SO2NH2, 249-50°, alc.-H2O; Me, H, SO2NH2, 239-41°, alc.-H2O; Me, H, SO2NHMe, 195-7°, alc.; H, H, SO2NMe2, 202-4°, alc.-H2O; H, H, MeSO2, 248-9°, alc.-H2O. The following 6-chloro-7-sulfamoyl-3,4-dihydro-2-substituted-1,2,4-benzothiadiazine 1,1-dioxides were obtained by ring closure of 5-chloro-2,4-disulfamoylaniline with the appropriate aldehyde. Acid cyclization was used for compds. no. 1, 2, and 9, and base cyclization for the remainder (compd. no., 2-substituent, m.p., and recrystn. solvent given): 1, Me, 252-3°, AcOH-H2O; 2, Et, 265°, AcOH-H2O; 3, CCl3, 287°, ethylene glycol monomethyl ether-H2O; 4, CH2OH, 225-6°, Me2CO-H2O; 5, oxiranyl, 233-5°, Me2CO-H2O; 6, (CH2)5, 259-60°, HCONMe2-H2O; 7, PhCH2, 260-2°, AcOH-H2O; 8, p-ClC6H4, 250-1°, AcOH-H2O; 9, p-O2NC6H4, 268-9°, Me2CO-Et2O; 10, 2-pyridyl, 260°, MeCN; 11, 5-nitro-2-furyl, 239-40°, Me2CO-Et2O. 5-Chloro-2,4-disulfamoylaniline (11.4 g.) in 20 ml. HCONMe2 and 17.6 g. CCl3CHO heated 24 hrs. on the steam bath, 100 ml. H2O added, and the solid repptd. from dil. NH4OH gave 14.5 g. 6-chloro-7-sulfamoyl-3-trichloromethyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide. When the reaction was carried out in 60 ml. HCONMe2 in the presence of 4.6 g. anhyd. KF 3 hrs. on the steam bath, 76% 6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 330°, was isolated, λ 225 and 279-80 mμ, ε 29,592 and 11,465. 5-Chloro-2,4-disulfamoylaniline (5.7 g.) and 5.9 g. cyclohexanone in 30 ml. HCONMe2 heated 2 hrs. with 2.3 g. anhyd. KF gave 7 g. 6-chloro-7-sulfamoyl-3,3-pentamethylene-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide. The following was illustrative of the method used for prepn. of 3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides. Compds. were recrystd. from aq. alc. in yields of 35-73%. 5-Chloro-2,4-disulfamoylaniline (8.4 g.) and 3.5 g. CO(NH2)2 was heated 45-60 min. at 200° (NH3 evolved), the solid cooled, dissolved in H2O, filtered, acidified, and recrystd. from aq. alc. The following compds. were thus obtained (substituents at 4, 5, 6, 7, and m.p. given): H, H, Cl, SO2NH2, 313°; H, Cl, H, SO2NH2, 314-15°; H, H, SO2NH2, Cl, 323-4°; H, H, Br, SO2NH2, 323-4°; H, H, Me, SO2NH2, 307-8°; H, H, MeO, SO2NH2, 291-3°; H, H, NO2, SO2NH2, above 350°; Me, H, Cl, SO2NH2, 315°. Ia (5.9 g.) in 25 ml. H2O contg. 0.88 g. NaOH shaken 10 min. with 3 g. Me2SO4 at room temp., the ppt. collected, washed, dried, and crystd. gave 2.8 g. 6-chloro-4-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (VII), m. 325-6° (Me2CO-alc.). VII heated 2.5 hrs. with 10% NaOH gave 5-chloro-2,4-disulfamoyl-N-methylaniline (VIII). Method (B). VIII (5 g.) in 70 ml. 98-100% HCO2H refluxed 24 hrs. and cooled to room temp. gave 4.7 g. VII. Ia (32.2 g.) added portionwise to 2.5 g. Na in 200 ml. alc., 16.3 g. CH2:CHCH2Br added, the soln. warmed 24 hrs. with intermittent addn. of 4 g. CH2:CHCH2Br after 6 hrs., and cooled gave 27.2 g. solids. Repeated extn. of this solid with Me2CO at room temp. gave 11.9 g. unchanged Ia and 12.5 g. 4-allyl-6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide

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(IX), m. 243-5° (aq.-alc.). IX (1 g.) in 20 ml. 10% NaOH heated 2 hrs. gave 0.5 g. 5-chloro-2,4-disulfamoyl-N-allylaniline (IXa), m. 181-3° (H2O). IX (1 g.) in 70 ml. H2O and 9 ml. N NaOH left 0.5 hr. at room temp., cooled, acidified, and the ppt. collected gave 0.4 g. 5-chloro-2-formylsulfamoyl-4-sulfamoyl-N-allylaniline (X), needles, m. 142.5-3.5° (CHCl3-Me2CO). Recrystn. of X from H2O gave IXa. 3,4-Dimethyl-1,2,4-benzothiadiazine 1,1-dioxide (11.4 g.) in 35 ml. ClSO3H heated 2.5 hrs. at 150-60°, poured onto ice, the solid added to 50 ml. concd. NH4OH, after 30-60 min. the product collected, and recrystd. gave 3,4-dimethyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 258-60° (HCONMe2-alc.). Repptn. of a sample from dil. NaOH gave 2-acetylsulfamoyl-4-sulfamoyl-N-methylaniline, m. 208-10° (Me2CO-ligroine). Ac2O (25 ml.) left overnight at room temp. with 8.9 g. Ia in 75 ml. C5H5N, the product collected, and dried gave 7.7 g. 7-acetylsulfamoyl-6-chloro-1,2,4-benzothiadiazine 1,1-dioxide (XI), m. 299° (rapid heating), pK'a 3.7, 7.2. XI (2 g.) in 10 ml. 10% NaOH heated 15 min., cooled, and acidified gave 4-acetylsulfamoyl-5-chloro-2-sulfamoylaniline (XII), plates, m. 221° (Me2CO-alc.). Cyclization of XII with HCO2H gave 7-acetylsulfamoyl-6-chloro-1,2,4-benzothiadiazine 1,1-dioxide. Butyric anhydride (25 ml.) left at room temp. overnight with 8.9 g. Ia in 75 ml. C5H5N, poured into ice H2O, and acidified gave 8.1 g. 7-butyrylsulfamoyl-6-chloro-1,2,4-benzothiadiazine 1,1-dioxide, m. 286° (alc.-H2O). Ia (10 g.) left 2 hrs. at room temp. with 50 ml. NHMe2, dissolved in 50 ml. 50% aq. alc., and acidified gave 5.8 g. 5-chloro-2-dimethylaminomethylenesulfamoyl-4-sulfamoylaniline, m. 208-10° (alc.-H2O). Ia (10 g.) and 13.6 g. piperidine heated 1 hr. on the steam bath, dild. with H2O, and acidified gave 3.8 g. 5-chloro-2-piperidinomethylenesulfamoyl-4-sulfamoylaniline, m. 210-12° (aq. alc.). Ia (29.6 g.) added portionwise to 150 ml. ClSO3H, the mixt. heated 2 hrs. on the steam bath, cooled, poured onto crushed ice, and the solid collected gave 30.3 g. 6-chloro-1,2,4-benzothiadiazine-7-sulfonyl chloride 1,1-dioxide (XIIa), m. 259-61° (Me2CO-hexane). 6-Chloro-2-methyl-7-methylsulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (68.3 g.) added portionwise to 200 ml. ClSO3H, the mixt. heated 5 hrs., cooled, poured onto ice, and collected gave 60 g. 5-chloro-2-methylsulfamoylaniline-4-sulfonyl chloride (XIII), m. 158° (effervescence) (Me2CO-C6H6). XIII (43.2 g.) added portionwise to 250 ml. concd. NH4OH, the mixt. heated 1 hr., concd., and the solid recrystd. gave 17.9 g. 5-chloro-2-methylsulfamoyl-4-sulfamoylaniline as 2 crystal modifications, m. 168-70° and 188-90°. XIIa (10 g.) added to 30 ml. MeNH2 and left at room temp. gave a residue, which dissolved in 200 ml. 5% NaOH, heated 2 hrs., and acidified gave 6.4 g. 5-chloro-4-methylsulfamoyl-2-sulfamoylaniline, m. 182-3° (H2O). XIIa (30 g.) left at room temp. with 150 ml. anhyd. NHMe2 gave 22.8 g. 5-chloro-2-dimethylaminomethylenesulfamoyl-4-dimethylsulfamoylaniline (XIV), m. 195-7° (alc.). XIV (6.7 g.) in 20 ml. 10% NaOH heated 1 hr. and acidified gave 4.0 g. 5-chloro-4-dimethylsulfamoyl-2-sulfamoylaniline, m. 158-60° (aq. alc.). Ia (3 g.) in 100 ml. MeOH reduced at room temp. and 39 lb./sq. in. initial H pressure over 1 g. 5% ruthenium-C, after 10 hrs. the mixt. heated, filtered, and concd. gave 83% 6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (XV). KMnO4 (3.75 g.) added

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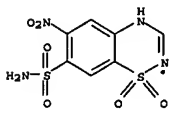
portionwise to 8.9 g. XV in 150 ml. H2O and 10 ml. 20% NaOH, the soln. stirred 15 min. at room temp., warmed 5 min. on the steam bath, excess KMnO4 destroyed with 2-3 ml. alc., and the soln. acidified gave 7.4 g. 6-chloro-7-sulfamoyl-1,2,4-benzothiadiazine. Similar oxidn. of 6-methyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide gave a comparable yield of 6-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 345°. 5-Chloro-2,4-bis(dimethylsulfamoyl)aniline (XVI) (3.4 g.) and 10 g. 50% PhCH2CHO in alc. heated 0.5 hr. at 150°, the mixt. cooled, and the solid triturated with MeCN gave 2.4 g. 5-chloro-2,4-bis(dimethylsulfamoyl)-N-(2-phenylethylidene)aniline, m. 203-5° (MeCN), λ 226-8 and 337-40 mμ, ε 27,351 and 36,106. XVI (3.4 g.), 3 g. p-O2NC6H4CHO, and 60 ml. PhMe refluxed 20 hrs., cooled, and the solid triturated with 200 ml. refluxing alc. gave 3.6 g. 5-chloro-2,4-bis(dimethylsulfamoyl)-N-(p-nitrobenzylidene)aniline, m. 221-3° (MeCN), λ 276-281 mμ, ε 25,270. The ultraviolet absorption spectra were given for a no. of 1,2,4-benzothiadiazine 1,1-dioxides and 5-chloro-2,4-disulfamoylanilines.

IT 23141-81-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide 23141-88-0, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-, 1,1-dioxide 47068-12-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide 100383-15-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-, 1,1-dioxide
(preparation of)

RN 23141-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 23141-88-0 CAPLUS
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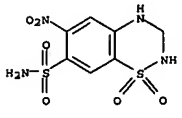
(6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



RN 47068-12-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide (6CI, 9CI) (CA INDEX NAME)

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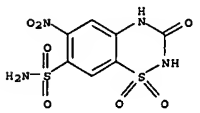

RN 100383-15-1 CAPLUS
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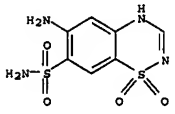
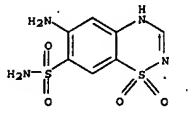


L4 ANSWER 31 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:34355 CAPLUS
DOCUMENT NUMBER: 54:34355
ORIGINAL REFERENCE NO.: 54:6770e-f
TITLE: Benzothiadiazine 1,1-dioxides
INVENTOR(S): Novello, Fred C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: Continuation-in-part of U.S. 2,809,194 (C.A. 52, 2939h)
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2910475		19591027	US 1957-683694	19570913

AB Substituted 7-sulfamylbenzothiadiazine 1,1-dioxide compds. may be prepared by heating benzothiadiazine 1,1-dioxide and ClSO3H and treating with NH3 or a primary or secondary amine. To 35 ml. ClSO3H is added 10 g. 3,4-dimethyl-1,2,4-benzothiadiazine 1,1-dioxide, heated 4 hrs. at 140-60°, cooled, poured onto ice, filtered, treated with 25 ml. 28% NH4OH at room temperature, cooled, filtered and water-washed to yield 3,4-dimethyl-7-sulfamyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 258-60° (Me2CO-petr. ether). Similarly prepared were: 7-sulfamyl-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 319-20° and 6-chloro derivative of I, m. 342.5-3.0°.
IT 100383-15-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-, 1,1-dioxide
(preparation of)
RN 100383-15-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-, 1,1-dioxide (6CI) (CA INDEX NAME)

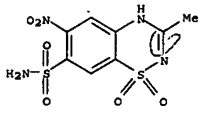


L4 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:23253 CAPLUS
DOCUMENT NUMBER: 54:23253
ORIGINAL REFERENCE NO.: 54:4636b-e
TITLE: 6-Nitro-7-sulfamoylbenzothiadiazine 1,1-dioxides
INVENTOR(S): Novello, Fred C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: Continuation-in-part of U.S. 2,809,194 (C.A. 52, 2939h)
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

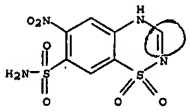
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2910473		19591027	US 1957-672126	19570716
FR 1383705			FR	
GB 891471			GB	

AB To 375 ml. ClSO3H is added 64 g. m-O2NC6-H4NH2 followed by 350 g. NaCl in 1-2 hrs., the mixture gradually heated to 150° and kept there 3 hrs., cooled 1 l. cold water added, the mixture extracted with Et2O (I), the extract water-washed, dried, the I recovered, the residue cooled and treated with 150 ml. 28% NH4OH, heated 1 hr. on the steam bath, cooled, the product filtered off, water-washed, and dried to give 2,4-disulfamoyl-5-nitroaniline (II), m. 260-2° (dilute alc.). II (5 g.) in 175 ml. 100% HCO2H is refluxed 3 hrs., cooled, filtered, and washed with EtOH to give 6-nitro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (III), m. 338-9°. III (2.7 g.) in 600 ml. 50% EtOH is shaken in a H atmospheric with 400 g. PrO2 catalyst to maximum H absorption, filtered, the solution evaporated to dryness in vacuo, and the residue crystallized from 50% EtOH to give 6-amino-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 323-4°. The compds. have diuretic and (or) natriuretic properties and are useful therapeutic agents.
IT 2850-46-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide 23141-81-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide 100383-15-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-, 1,1-dioxide 103151-36-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-propyl-, 1,1-dioxide 105143-42-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-pentyl-, 1,1-dioxide 106273-76-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-phenyl-, 1,1-dioxide 106379-57-1, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-benzyl-, 1,1-dioxide 107149-74-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-methyl-, 1,1-dioxides
(preparation of)
RN 2850-46-6 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-methyl-6-nitro-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)

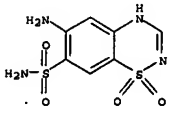
L4 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



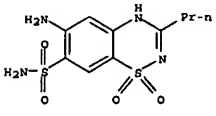
RN 23141-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-nitro-, 1,1-dioxide (6CI, 8CI, 9CI) (CA INDEX NAME)



RN 100383-15-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-, 1,1-dioxide (6CI) (CA INDEX NAME)

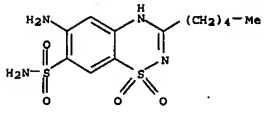


RN 103151-36-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-propyl-, 1,1-dioxide (6CI) (CA INDEX NAME)

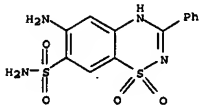


RN 105143-42-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-pentyl-, 1,1-dioxide (6CI) (CA INDEX NAME)

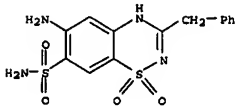
L4 ANSWER 32 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



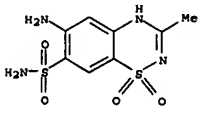
RN 106273-76-1 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-phenyl-, 1,1-dioxide (6CI) (CA INDEX NAME)



RN 106379-57-1 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-benzyl-, 1,1-dioxide (6CI) (CA INDEX NAME)



RN 107149-74-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3-methyl-, 1,1-dioxide (6CI) (CA INDEX NAME)



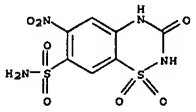
L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1959:99992 CAPLUS
DOCUMENT NUMBER: 53:99992
ORIGINAL REFERENCE NO.: 53:18075i,18076a-b
TITLE: 3-Oxo-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide compounds
INVENTOR(S): Novello, Frederick C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2886566		19590512	US	

AB The title compds. (I), with diuretic and (or) natriuretic properties, were prepared 5,2,4-Cl(H2NO2S)2C6H2NH2 [for the sulfamoyl anilines, cf. U.S. 2,809,194 (C.A. 52, 2939h)] (8.4 g.) and 3.5 g. urea heated 40 min. at 200° in an oil bath, the mixture cooled, the solid dissolved in H2O, the solution filtered, the filtrate acidified, and the precipitate crystallized (aqueous EtOH) gave 4.3 g. 6-chloro-3-oxo-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 313° (decomposition) (previous darkening). Similarly were prepared the following substituted I (substituent and m.p. (decomposition) (previous darkening) given): 5-Cl, 314-15°; 6-Br, 323-4°; 6-Me, 307-8°; 6-MeO, 291-3°; 6-O2N (II), above 350°; 6-H2N (by catalytic reduction of II), -; 7-Cl, 323-4°.

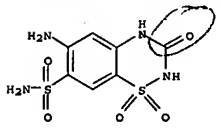
IT 47068-12-2, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide 100383-17-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-3-oxo-, 1,1-dioxide
(preparation of)

RN 47068-12-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-6-nitro-3-oxo-, 1,1-dioxide (6CI, 9CI) (CA INDEX NAME)



RN 100383-17-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-amino-3,4-dihydro-3-oxo-, 1,1-dioxide (6CI) (CA INDEX NAME)

L4 ANSWER 33 OF 33 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



(2)

isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
12:CLASS 13:CLASS 14:Atom 15:CLASS

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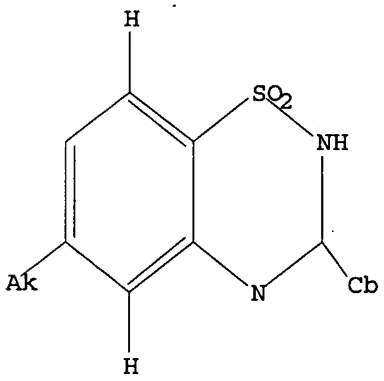

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100.0% PROCESSED 656 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 11584 TO 14656
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

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FULL SCREEN SEARCH COMPLETED - 13037 TO ITERATE

100.0% PROCESSED 13037 ITERATIONS 78 ANSWERS
SEARCH TIME: 00.00.01

L3 78 SEA SSS FUL L1

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COST IN U.S. DOLLARS SINCE FILE TOTAL

	ENTRY	SESSION
FULL ESTIMATED COST	166.94	167.15

FILE 'CAPLUS' ENTERED AT 08:35:40 ON 06 NOV 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 6 Nov 2006 VOL 145 ISS 20
FILE LAST UPDATED: 5 Nov 2006 (20061105/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 21 L3

=> d ibib abs hitstr tot

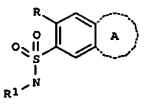
L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:850385 CAPLUS
DOCUMENT NUMBER: 145:293109
TITLE: Preparation of nitric oxide enhancing diuretic compounds, compositions and methods of use
INVENTOR(S): Garvey, David S.; Letts, L. Gordon; Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Gaston, Ricky D.; Khanapure, Subhash P.; Lin, Chia-En; Ranatunge, Ramani R.; Stevenson, Cheri A.; Wey, Shiow-Jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 91pp., which which which which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006189603	A1	20060824	US 2006-360599	20060224
WO 2006091716	A2	20060831	WO 2006-US6375	20060224
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.:
US 2005-655414P P 20050224
US 2005-656545P P 20050228
US 2005-685027P P 20050526
US 2005-692228P P 20050621
US 2005-749853P P 20051213

OTHER SOURCE(S): MARPAT 145:293109
GI

L4 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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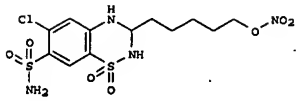
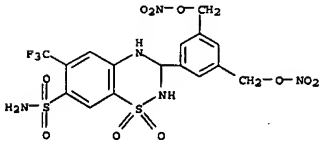


II

AB The invention describes novel compns. and kits comprising at least one nitric oxide enhancing diuretic compound I [R = Cl or CF3; R1 = H, alkyl, cycloalkyl, etc.; Ring A = substituted heterocycle], or pharmaceutically acceptable salts thereof, and, optionally, at least one nitric oxide enhancing compound and/or at least one therapeutic agent. Methods for preparing I are provided. Thus, e.g., II was prepared by cyclocondensation of 6-(nitrooxy)hexanal (preparation given) with 2-amino-6-chloro-1,3-benzenedisulfonamide. Assays for determining diuresis are described (data given). The invention also provides methods for (a) treating conditions resulting from excessive water and/or electrolyte retention; (b) treating cardiovascular diseases; (c) treating renovascular diseases; (d) treating diabetes; (e) treating diseases resulting from oxidative stress; (f) treating endothelial dysfunctions; (g) treating diseases caused by endothelial dysfunctions; (h) treating cirrhosis; (j) treating pre-eclampsia; (k) treating osteoporosis; (l) treating nephropathy; (m) treating peripheral vascular diseases; (n) treating portal hypertension; (o) treating central nervous system disorders; (p) treating metabolic syndrome; (q) treating sexual dysfunctions; and (r) hyperlipidemia. The nitric oxide enhancing diuretic compds. comprise at least one nitric oxide enhancing group linked to the diuretic compound through one or more sites such as carbon, oxygen and/or nitrogen via a bond or moiety that cannot be hydrolyzed.

IT 907624-13-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiadiazine nitric oxide derivs. as diuretics)

RN 907624-13-9 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-[3,5-bis[(nitrooxy)methyl]phenyl]-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)



own work

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:549265 CAPLUS
DOCUMENT NUMBER: 131:184974
TITLE: Preparation of benzothiadiazines, quinazolines, and other aryl-fused heterocycles as positive AMPA-receptor modulators for treatment of memory and learning disorders
INVENTOR(S): Gouliaev, Alex Haahr; Larsen, Mogens; Varming, Thomas; Mathiesen, Claus; Johansen, Tina Holm; Scheel-Kruger, Jorgen; Olsen, Gunnar M.; Nielsen, Elsebet Ostergaard
PATENT ASSIGNEE(S): Neurosearch A/S, Den.
SOURCE: PCT Int. Appl., 168 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9942456	A2	19990826	WO 1999-DK70	19990218
WO 9942456	A3	19991007		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
ZA 9609414	A	19970612	ZA 1996-9414	19961108
CA 2320354	AA	19990826	CA 1999-2320354	19990218
AU 9925123	A1	19990906	AU 1999-25123	19990218
AU 751384	B2	20020815		
ZA 9901301	A	19990913	ZA 1999-1301	19990218
TR 200002427	T2	20010122	TR 2000-200002427	19990218
EP 1071426	A2	20010131	EP 1999-904730	19990218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
JP 2002504481	T2	20020212	JP 2000-532408	19990218
EE 200000468	A	20020415	EE 2000-468	19990218
RU 2214405	C2	20031020	RU 2000-121882	19990218
NO 2000004121	A	20001017	NO 2000-4121	20000817
US 6943159	B1	20050913	US 2000-641814	20000818
US 2004043987	A1	20040304	US 2003-642224	20030818

PRIORITY APPLN. INFO.:
DK 1998-226 A 19980218
WO 1999-DK70 W 19990218
US 2000-641814 A3 20000818

OTHER SOURCE(S): MARPAT 131:184974
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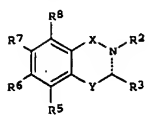
L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



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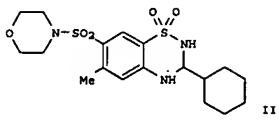


II

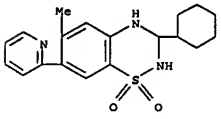
AB Benzothiadiazines, quinazolines, and other aryl-fused heterocycles (I) [wherein the bond represented by the broken line may be a single, double bond, or absent; and if the bond is absent, then the N is substituted with a H and R2; X = SO2, CO, or CH2; Y = -CH(R4)-, -N(R4)-, -N(R4)-CH2-, or O; R2, R4 = H, alkyl, cycloalkyl, aryl, benzyl, substituted carbonyl, or taken together with R3 = (un)substituted 4-7 membered ring; R3 = H, (un)substituted cycloalkyl, (un)substituted alkyl, (un)substituted alkoxy, acyl, or taken together with R2 or R4 = (un)substituted 4-7 membered ring, etc.; R5 = H, halogen, alkyl, alkenyl, alkynyl, aryl, or (un)substituted sulfonamido; R6, R7, R8 = H, halogen, (un)substituted alkyl, CN, cyanoalkyl, NO2, (un)substituted alkoxy, (un)substituted sulfonamido, (un)substituted aryl, etc.] were prepared as pos. AMPA-receptor modulators for treatment of memory and learning disorders. Thus, ClSO2NCO was added to a cooled solution of m-toluidine and nitroethane or nitromethane followed by addition of AlCl3 and reaction with H2SO4 to form a mixture of 2-amino-6-methylbenzenesulfonamide and 2-amino-4-methylbenzenesulfonamide. The latter isomer was separated by recrystn. and cyclized with cyclohexanecarbonyl chloride in a mixture of TEA, 4-(N,N-dimethylamino)pyridine, and THF to yield dihydro-3-cyclohexyl-6-methyl-1,2,4-benzothiadiazine-1,1-dioxide. The dihydrobenzothiadiazine-1,1-dioxide was chlorosulfonated with chlorosulfonic acid, sulfamoylated with morpholine, and reduced with DIBALH in toluene to give 3-cyclohexyl-6-methyl-7-morpholinosulfonyl-1,2,3,4-tetrahydro-1,2,4-benzothiadiazine-1,1-dioxide (II). Selected compds. of the invention were tested for in vitro inhibition of 3H-AMPA binding and exhibited IC50 values ranging from 3.4 μM to 45 μM. Two compds. were tested and showed significantly increased potentiation of AMPA-induced [3H]GABA release from cultured cortical neurons relative to the potentiation induced by 30 μM cyclothiazide. Expts. were performed in voltage clamp, and all tested compds. reversibly potentiated the current induced by application of 30 μM AMPA. The results of iontophoretic application showed that cyclothiazide did not exhibit any in vivo effects after i.v. administration but that five compds. of the invention enhanced AMPA evoked spike activity in an activity-dependent manner. Passive avoidance expts.

L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

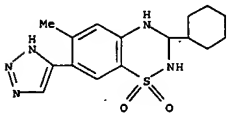
were performed to test the pharmacol. effect of compds. on associative memory. Mean entry latency results for each group and the memory enhancing effect of different concns. of one compd. were given.

IT 240139-57-5P 240139-58-6P 240139-59-7P
240139-60-0P 240139-61-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzothiadiazines, quinazolines, and other aryl-fused heterocycles as pos. AMPA-receptor modulators for treatment of memory and learning disorders)

RN 240139-57-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 3-cyclohexyl-3,4-dihydro-6-methyl-7-(2-pyridinyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

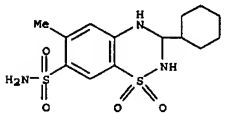


RN 240139-58-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 3-cyclohexyl-3,4-dihydro-6-methyl-7-(1H-1,2,3-triazol-4-yl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

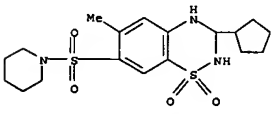


RN 240139-59-7 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-methyl-, 1,1-dioxide (9CI) (CA INDEX NAME)

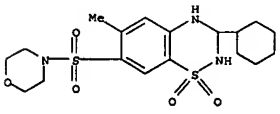
L4 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 240139-60-0 CAPLUS
CN Piperidine, 1-[(3-cyclopentyl-3,4-dihydro-6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

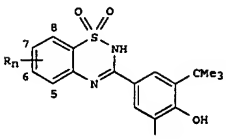


RN 240139-61-1 CAPLUS
CN Morpholine, 4-[(3-cyclohexyl-3,4-dihydro-6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-7-yl)sulfonyl]- (9CI) (CA INDEX NAME)

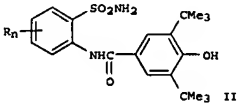


L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:589565 CAPLUS
DOCUMENT NUMBER: 125:328676
TITLE: Synthesis and free radical scavenging activity of 4-(2H-1,2,4-benzothiadiazine-1,1-dioxide-3-yl)-2,6-bis(1,1-dimethylethyl)phenols
AUTHOR(S): Tait, Annalisa; Ganzerli, Stefano; Bella, Maria Di
CORPORATE SOURCE: Dip. Sci. Farmaceutiche, Univ. Modena, Modena, 4100, Italy
SOURCE: Tetrahedron (1996), 52(38), 12587-12596
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



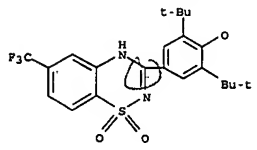
II

AB Title compds. I [Rn = 6-Br, 7-Br, 5,7-Br2, 6,7-Br2, 6-Cl, 7-Cl, 5,7-Cl2, 6-CF3, 6-Me, 6-OMe, 7-NO2], with potential biol. activity as antioxidants, were prepared in 30-77% yield by cyclization of the corresponding bis(dimethylethyl)hydroxy(sulfamoylphenyl)benzamides II, either neat at 230° or in boiling aqueous NaOH. I and II were tested as free-radical scavengers by reaction with DPPH using UV and ESR spectrometry. The formation of stable phenoxy radicals, obtained by oxidation of I and II with Pb(OAc)4, was also studied.

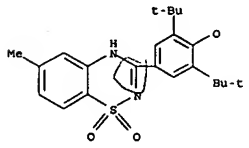
IT 183295-99-0P 183296-00-6P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(ESR of; preparation and free radical-scavenging activity of benzothiadiazinylbis(dimethylethyl)phenols)

RN 183295-99-0 CAPLUS
CN Phenoxy, 2,6-bis(1,1-dimethylethyl)-4-[1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]- (9CI) (CA INDEX NAME)

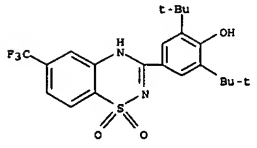
L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 183296-00-6 CAPLUS
CN Phenoxy, 2,6-bis(1,1-dimethylethyl)-4-(6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl)- (9CI) (CA INDEX NAME)

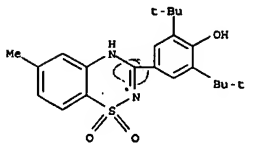


IT 183295-54-7P 183295-56-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and free radical-scavenging activity of benzothiadiazinylbis(dimethylethyl)phenols)
RN 183295-54-7 CAPLUS
CN Phenol, 2,6-bis(1,1-dimethylethyl)-4-[1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]- (9CI) (CA INDEX NAME)



RN 183295-56-9 CAPLUS

L4 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Phenol, 2,6-bis(1,1-dimethylethyl)-4-(6-methyl-1,1-dioxido-2H-1,2,4-benzothiadiazin-3-yl)- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1984:175285 CAPLUS
DOCUMENT NUMBER:	100:175285
TITLE:	Substituted 4-phenoxy and 4-phenylthio prolines
INVENTOR(S):	Haugwitz, Rudiger D.; Sprague, Peter W.
PATENT ASSIGNEE(S):	E. R. Squibb and Sons, Inc., USA
SOURCE:	Eur. Pat. Appl., 99 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

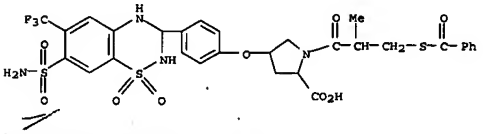
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 95584	A2	19831207	EP 1983-104221	19830429
EP 95584	A3	19840328		
EP 95584	B1	19870107		
R: BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
ZA 8302762	A	19831228	ZA 1983-2762	19830419
CA 1258853	A1	19890829	CA 1983-426141	19830419
AU 8313837	A1	19831103	AU 1983-13837	19830421
US 4681886	A	19870721	US 1983-488491	19830425
JP 58203987	A2	19831128	JP 1983-76078	19830428
JP 04032071	B4	19920528		
PRIORITY APPLN. INFO.:			US 1982-373570 A	19820430

OTHER SOURCE(S): CASREACT 100:175285; MARPAT 100:175285
GI

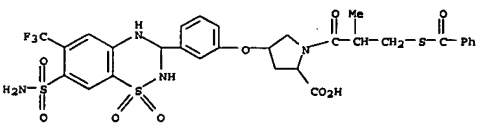
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S; X1, X2 = CHNH, C:N; X3 = CO, SO2; R = H, alkyl, CH2Ph, CHPh2, cation; R1, R2 = H, halo, alkyl, alkoxy, haloalkyl, NO2, SO2NH2; R3 = H, alkyl, cycloalkylalkyl, (un)substituted phenylalkyl, haloalkyl, hydroxyalkyl; R4 = R5SCH2CHR6CO (R5 = H, acyl; R6 = H, alkyl, haloalkyl, Ph, CH2Ph, CH2CH2Ph, cycloalkyl), R8O2CCH2CH2NR7CO (R7 = alkyl, cycloalkyl; R8 = same as R), R9O2CCHR10NHCHR11CO [R9 = same as R; R10 = H, (CH2)mC6H4R12 (R12 = H, alkyl, alkoxy, halo, OH; m = 0-4), (un)substituted alkyl; R11 = H, (CH2)mR12, (un)substituted alkyl], R13P(O)(OR14)CH2CO [R13 = alkyl, (CH2)nR15 [R15 = C6H4R12, thienyl, furyl, pyridyl, cycloalkyl; n = 0-7]; R14 = H, alkyl, CH2Ph, CHPh2, ion, CHR17O2CR16 (R16 = H, alkyl, alkoxy, cycloalkyl, Ph, CH2Ph, CH2CH2Ph; R17 = H, alkyl, cycloalkyl, Ph)]] were prepared as antihypertensives (no data) due to their ability to inhibit angiotensin-converting enzyme. Thus, L-4-hydroxyproline was acylated with D-BzSCH2CHMeCOCl to give BzSCH2CHMeCO-Hyp-OH, which was esterified with MeOH/p-MeC6H4SO3H to give the Me ester, which was treated with m-HOC6H4CH(OMe)2 in the presence of Ph3P to give hydroxyproline II. The cyclocondensation of II with benzamide III gave quinazoline IV (R18 = Bz, R19 = Me), which was sapond. to give IV (R18 = R19 = H).

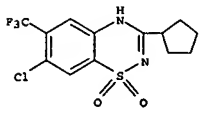
L4 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
IT 89813-52-5P 89813-53-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 89813-52-5 CAPLUS
CN L-Proline, 4-[4-[7-(aminosulfonyl)-3,4-dihydro-1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2α,4α)- (9CI) (CA INDEX NAME)



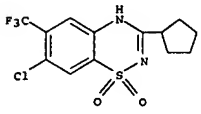
RN 89813-53-6 CAPLUS
CN L-Proline, 4-[3-[7-(aminosulfonyl)-3,4-dihydro-1,1-dioxido-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-3-yl]phenoxy]-1-[3-(benzoylthio)-2-methyl-1-oxopropyl]-, (2α,4α)- (9CI) (CA INDEX NAME)



L4 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1973:400114 CAPLUS
DOCUMENT NUMBER: 79:114
TITLE: Correlation between the antihypertensive activity and the structure of 2H-1,2,4-benzothiadiazine 1,1-dioxide. Comparison of the parametric and topologic treatments
AUTHOR(S): Aranda, Antoinette
CORPORATE SOURCE: Lab. Chim. Org. Phys., Univ. Paris VII, Paris, Fr.
SOURCE: Comptes Rendus des Seances de l'Academie des Sciences,
Serie C: Sciences Chimiques (1973), 276(15), 1301-4
CODEN: CHDCAQ; ISSN: 0567-6541
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The antihypertensive activity of a series of 2H-1,2,4-benzothiadiazine 1,1-dioxides was analyzed using the topol. DARC-PELCO method (1966) and the parametric method of Topliss and Yudis (1972). The predictive value of the DARC-PELCO method was also examined
IT 38726-94-2
RL: BIOL (Biological study)
(antihypertensive)
RN 38726-94-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 7-chloro-3-cyclopentyl-6-(trifluoromethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1973:92400 CAPLUS
DOCUMENT NUMBER: 78:92400
TITLE: Structure-activity correlation in a series of 2H-1,2,4-benzothiadiazine 1,1-dioxides
AUTHOR(S): Tinland, B.; Decoret, C.; Badin, J.
CORPORATE SOURCE: Lab. Spectrosc. Lumin., Univ. Lyon I, Villeurbanne, Fr.
SOURCE: Pharmacological Research Communications (1972), 4(3), 195-9
CODEN: PLRCAT; ISSN: 0031-6989
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The observed and calculated activity values were highly correlated for compds.
such as 6,7-dibromo-3-isopropyl-2H-1,2,4-benzothiadiazine 1,1-dioxide (I) [38726-93-1], 7-chloro-3-cyclopentyl-6-trifluoromethyl-2H-1,2,4-benzothiadiazine 1,1-dioxide (II) [38726-94-2], 7-chloro-3-isopropyl-6-methyl-2H-1,2,4-benzothiadiazine 1,1-dioxide (III) [38726-95-3], and 3-(2-thienylmethyl-6-trifluoromethyl-2H-1,2,4-benzothiadiazine 1,1-dioxide (IV) [38726-96-4] using the antihypertensive activity data determined by Toplis and Yudis (1972) and the Free-Wilson approach (1964) to structure-activity studies. The maximum antihypertensive
activities for yet unsynthesized compds. could be predicted with this model which suggested that a compound containing the substituents R1 = Δ3-cyclopentenyl, R2 = Br, R3 = CF3, R4 = CF3, and R5 = Cl would be most active.
IT 38726-94-2
RL: BIOL (Biological study)
(antihypertensives)
RN 38726-94-2 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 7-chloro-3-cyclopentyl-6-(trifluoromethyl)-, 1,1-dioxide (9CI) (CA INDEX NAME)

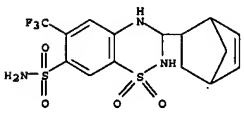


L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1967:10970 CAPLUS
DOCUMENT NUMBER: 66:10970
TITLE: 7-Sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide derivatives
INVENTOR(S): Mueller, Erich; Hasspacher, Klaus
PATENT ASSIGNEE(S): Boehringer Ingelheim G.m.b.H.
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3275625		19660927	US	19610123

GI For diagram(s), see printed CA Issue.
AB Novel derivs. of 7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, which are substituted in the 3-position by an alicyclic bicyclic radical, can be prepared by the following process. A mixture of 8.5
g. 6-chloro-4-aminobenzene-1,3-disulfonamide, 4 g. 2,5-endomethylene-Δ3-tetrahydrobenzaldehyde, and 25 cc. diethylene glycol dimethyl ether was heated 2 hrs. at 100° and the mixture allowed to stand 14 hrs. at room temperature to give 7.5 g. 3-(bicyclo[2,2,1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 229-30°. Similarly were prepared the following compds.: 3-(bicyclo[2.2.1]hept-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 263-6°; 3-(2,3-dibromobicyclo[2.2.1]hept-6-yl)-6-chloro-7-sulfamoyl-3,4,dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 199-201°C. (decomposition); 3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-trifluoromethyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 119°; 3-(bicyclo[2.2.1]hept-2-en-6-yl)-5-methyl-6-chloro-7-sulfamoyl-3-4,dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m 190-1°; 3-(bicyclo[2.2.1]hept-2-en-6-yl)-5,6-dichloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m.
184°; 2-methyl-3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-methylsulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 232-5°; 3-(bicyclo[2.2.2]oct-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 276-7° (decomposition): 3-(5-methylbicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 197-9°; 3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide, m. 226-30°. Coated pills, suppositories, gelatin capsules, and liquid-containing ampuls are made from
the various diuretic compds.
IT 859-24-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 859-24-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

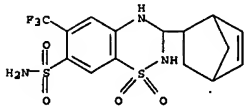


L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:498466 CAPLUS
DOCUMENT NUMBER: 63:98466
ORIGINAL REFERENCE NO.: 63:18126e-h,18127a
TITLE: 7-Sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides
INVENTOR(S): Thomae, Karl
PATENT ASSIGNEE(S): G.m.b.H.
SOURCE: 12 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

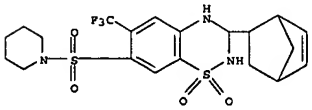
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
NL 296964		19650525	NL	
PRIORITY APPLN. INFO.:			DE	19620824

GI For diagram(s), see printed CA Issue.
AB The title compds. (I), useful as diuretics, are prepared Thus, to a solution of 16.28 g. 6-chloro-4-aminobenzene-1,3-disulfonyl chloride (II) in 50 ml. dry tetrahydrofuran (THF) is added dropwise at 20° under cooling 25 ml. of a solution containing 12.28 g. MeNH2 in 100 ml. THF. The mixture is diluted with 50 ml. acetone, filtered, and evaporated in vacuo at 20°. The oily residue is recrystd. twice from 260 ml. 1:1 MeOH-H2O at -10° to yield 3-methylsulfonamido-4-amino-6-chlorobenzenesulfonyl chloride (III), m. 146-8°. Similarly prepared are the following IV (R4, R5, R8, and m.p. given): Cl, H, H, 166-7° (V) (78.7% yield); CF3, H, H, 161-3° (VI); Cl, H, benzyl, 135-8° (CHCl3,) (VII) (62% yield). To a solution of 1.6 g. III and 15 mg. p-toluenesulfonic acid in dioxane is added at 70° 0.61 g. 2,5-endomethylene-1,2,5,6-tetrahydrobenzaldehyde (VIII); the mixture is held 20 min. at 70° and worked up to yield 2-methyl-3-(bicyclo [2.2.1] hept-2-en-6-yl)-6-chloro-7-chlorosulfonyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (IX), decomposed at 154-9° (MeOH-H2O). Similarly, V, VI, and VII are converted with VIII into the corresponding 3-(bicyclo [2.2.1] hept-2-en-6-yl) - 7- chlorosulfonyl-3,4-dihydro - 1,2,4 -benzothiadiazine 1,1-dioxides (R4, R5, R8, and m.p. given): Cl, H, H, 186-7° (MeOH-H2O) (X); CF3, H, H, -(XI); Cl, H, benzyl, 188-9° (decomposition) (XII). A solution of 1 g. IX in 25 ml. THF is treated 15 min. with gaseous NH3 to yield 2-methyl-3-(bicyclo[2.2.1]hept-2-en-6-yl)-6-chloro-7-sulfonamido-3,4-dihydro - 1,2,4 - benzothiadiazine 1,1-dioxide, m. 257-8° (EtOH-H2O). Similarly prepared are the 3-(bicyclo[2.2.1]hept-2-en-6-yl)-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I)(R1 : R2 : R3 : R5 : H) (R4, R6, R7, R8, and m.p. given): Cl, Me, H, Me, 231-3° (MeOH-H2O); Cl, Me, H, H (XIII), 212-14° (MeOH-H2O); Cl, H, H, H, 226-8° (MeOH-H2O); CF3, R6R7 : piperidino, H, 133-40° (decomposition); CF3, H, H, H, 165-8°; Cl, H, H, H, benzyl, 222-4° (decomposition). A solution of 0.808 g. XIII in dioxane is

L4 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
reduced with H and Raney Ni to yield 3-(bicyclo[2.2.1]hept-6-yl)-6-chloro-7- (N-methylsulfonamido)-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 246-8°.
IT 859-24-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide
4233-37-8, Piperidine, 1-[[3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]-, S,S-dioxide
(preparation of)
RN 859-24-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



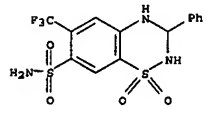
RN 4233-37-8 CAPLUS
CN Piperidine, 1-[[3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-2H-1,2,4-benzothiadiazin-7-yl]sulfonyl]-, S,S-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:51748 CAPLUS
DOCUMENT NUMBER: 62:51748
ORIGINAL REFERENCE NO.: 62:9157e-g
TITLE: 1,2,4-Benzothiadiazine derivatives
INVENTOR(S): Novello, Frederick C.
PATENT ASSIGNEE(S): Merck & Co., Inc.
SOURCE: 2 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3160629		19641208	US 1961-101331	19610407
PRIORITY APPLN. INFO.:			US	19610407

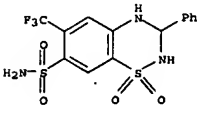
GI For diagram(s), see printed CA Issue.
AB A process leading to the title compds. is described. Thus, 3.75 g. KMnO4 is added with stirring over 10 min. to a solution of 8.9 g. 6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide in 150 ml. H2O and 10 ml. 20% NaOH. The solution is stirred at room temperature 15 min. and warmed on a steam bath 5 min., EtOH added to destroy excess KMnO4, and the solution filtered and acidified to give 6- chloro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 337°. Similarly prepared is 6-methyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, m. 345°.
IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
(preparation of)
RN 1170-25-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1965:51747 CAPLUS
DOCUMENT NUMBER: 62:51747
ORIGINAL REFERENCE NO.: 62:9157c-e
TITLE: Benzothiadiazine dioxides
INVENTOR(S): Cheney, Lee C.; Holdrege, Charles T.
PATENT ASSIGNEE(S): Bristol Laboratories International, S. A.
SOURCE: 18 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
FR 1368708		19640807	FR 1959-806279	19590929
US 3230218		19660118	US 1959-795595	19590226
PRIORITY APPLN. INFO.:			US	19580930

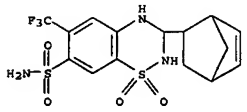
OTHER SOURCE(S): MARPAT 62:51747
GI For diagram(s), see printed CA Issue.
AB The title compds. (I) are used for the treatment of edemas associated with cardiac congestion, cirrhosis of the liver and kidney, and other diseases characterized by excessive accumulation of water. These compds. are obtained by the condensation of an aldehyde with a suitable aniline derivative Thus, to a solution of 0.09 mole 2-tri-fluoromethyl-4-amino-5-sulfamoylbenzenesulfonyl chloride in 125 cc. dioxane was added 15 cc. 40% CH2O, the solution added to 125 cc. concentrated NH4OH, NH4OH distilled after 1.5 hrs., and the residue refluxed 2.5 hrs. to give I (R = R1 = H), m. 260-4°. The following I were similarly prepared (R, R1, and m.p. given): Me, Me, 216-21°; H, Et, 256-8° (decomposition) and 262-3° (decomposition) (2 forms); H, Me, 247-50° (decomposition); H, PhCH2, 221-3°; H, 2-pyridyl, 310-11°; H, Cl3C, 283-5° (decomposition); H, Ph, 219-21°. By using cyclohexanone ethylene acetal, 7-sulfamoyl-6-trifluoromethylspiro [2H-1,2,4-benzothiadiazine-3,1'-cyclohexane] 1,1-dioxide, m. 260-2°, was obtained.
IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
(preparation of)
RN 1170-25-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:462475 CAPLUS
DOCUMENT NUMBER: 59:62475
ORIGINAL REFERENCE NO.: 59:11536h,11537a-b
TITLE: Dihydrohenzothiadiazine dioxides
PATENT ASSIGNEE(S): Eli Lilly & Co.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

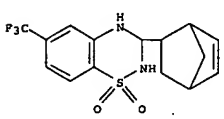
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 915236		19630109	GB	
PRIORITY APPLN. INFO.:			US	19601031

GI For diagram(s), see printed CA Issue.
AB The preparation of 3-(bicyclo[2.2.1]hept-2-en-5-yl)-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I) is described. These compds. are used as diuretic agents. 5-Chloro-2,4-disulfamoylaniline (28.5 g.) was suspended in 195 ml. 95% aqueous EtOH and 150 ml. 6N aqueous HCl, and 12.2 g. bicyclo[2.2.1]hept-2-en-5-ylcarboxaldehyde added, and the reaction stirred to effect solution of the aldehyde. The mixture was kept at room temperature 12 hrs. and the precipitate of I (R = Cl) filtered off and washed to remove HCl, m. 230-1° (EtOAc). Similarly prepared was I(R = CF3), m. 221°. These compds. were also prepared by cyclizing bicyclo[2.2.1]hept-2-en-5-ylcarboxaldehyde with 1,3-disulfamoyl-4-fluoro-6-chloro(or 6-trifluoromethyl)benzene in the presence of NH8 or by acylating 1,3-disulfamoyl-4-amino-6-chloro- (or trifluoromethyl)benzene with an anhydride or acid halide of bicyclo[2.2.1]hept-2-enyl-5-carboxylic acid, cyclizing the acylated product produced with an alkali, and then reducing the benzothiadiazine cyclization product to form a dihydrobenzothiadiazine.
IT 859-24-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (preparation of)
RN 859-24-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

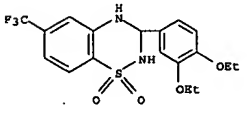


L4 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

L4 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:73334 CAPLUS
DOCUMENT NUMBER: 58:73334
ORIGINAL REFERENCE NO.: 58:12563c-d
TITLE: Hypotensive 1,2,4-benzothiadiazines
AUTHOR(S): Bierbaum, Barbara Ann; Traverso, John J.; Whitehead, Calvert W.
CORPORATE SOURCE: Lilly Res. Labs., Indianapolis, IN
SOURCE: Journal of Medicinal Chemistry (1963), 6, 272-5
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 58:73334
GI For diagram(s), see printed CA Issue.
AB 2-Aminobenzenesulfonamides were prepared by way of (1) the chlorosulfonation of aminobenzenes, (2) the amination of 2-chlorobenzenesulfonamides, and (3) the chlorine oxidation of 2-benzylthionitrobenzenes. New 1,2,4-benzothiadiazine 1,1-dioxides (I) were obtained by the cyclization of the 2-aminobenzenesulfonamides with formic acid, ortho esters, mixed anhydrides, and with aldehydes. The hypotensive activities of the endocyclic sulfonamides are described.
IT 852-16-4, 2H-1,2,4-Benzothiadiazine, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide 1828-19-9, 2H-1,2,4-Benzothiadiazine, 3-(3,4-diethoxyphenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (preparation of)
RN 852-16-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

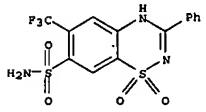


RN 1828-19-9 CAPLUS
CN 2H-1,2,4-Benzothiadiazine, 3-(3,4-diethoxyphenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

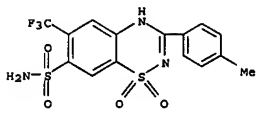


L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:53284 CAPLUS
DOCUMENT NUMBER: 58:53284
ORIGINAL REFERENCE NO.: 58:9078c-h
TITLE: Synthesis of 1,2,4-benzothiadiazine 1,1-dioxide derivatives
AUTHOR(S): Klosa, Josef
CORPORATE SOURCE: Privatlab., Berlin
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1962), 18, 313-20
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 58:53284
GI For diagram(s), see printed CA Issue.
AB The acylation of 5-trifluoromethylaniline-2,4-disulfonamides with carboxylic acids in the presence of POCl3 and subsequent cyclization of the resulting acylanilide analogs with concentrated H2SO4 yielded a series of 3-substituted 6-trifluoro-7-aminosulfonyl-1,2,4-benzothiadiazine 1,1-dioxides. 5,2,4-CF3(H2NO2S)C6H2NH2 (I) (6.4 g.), 2 cc. AcOH, and 6 cc. POCl3 heated 10-15 min. with stirring at 60-70° and then to 90-110°, cooled, diluted with 50 cc. H2O, boiled, cooled, and filtered yielded 6.7 g. N-Ac derivative (II) of I, leaflets, m. 292-4° (80% iso-PrOH) with browning from 250°. I (6.4 g.) in 30 cc. MePh and 2 cc. AcOH refluxed, treated during 15 min. dropwise with 6 cc. POCl3, refluxed 1 hr., cooled, and filtered, and the residue treated with 30 cc. H2O, heated on the water bath, and worked up in the usual manner yielded 6.8 g. II. Similarly were prepared the following III (R and m.p. given): EtCO, 312-14° (80% iso-PrOH); PrCO, 295-7° (needles); iso-PrCO, 282-4° (60% iso-PrOH); iso-BuCO, 208-10° (gray crystal powder); C7H15CO, 158-60° ClCH2CO, 298-300° (with browning from 250°); Cl2CHCO, 208-10° [resolidified at 220° and remelted at 296-8° (decomposition)]; CCl3CO, 228-30° [resolidified at 234° and remelted at 293-5° (decomposition)] CH2BrCO, 228-30° (resolidified at 250°); CHBr2CO, 220-2° (with browning at 210° (decomposition); MeCHBrCO, 304-6° with sintering an turning brown-yellow from 250°; Me2CHCHBr, 128-30° (needles); Bz, 250-2° (resolidified at 270° and decompose at 328-30°]; p-MeOC6H4CO, m. 246-8° (resolidified at 260° and decomposed up to 290°); 3,4,5-(MeO)3C6H2CO, 212-14°; p-MeC6H4CO, 165-7° with browning from 250° (needles); PhCH2CO, 134-6° (80% iso-PrOH); Ph2CHCO, 228-30° (needles); EtPhCHCO, 162-4° (crystal powder); picolinoyl, 158-60° (crystal powder); nicotinoyl, 226-8° (needles); isonicotinoyl, 233-5° (needles). II (6 g.) added in portions with stirring to 20-30 cc. concentrated H2SO4, heated 2-3 hrs. at 60-70°, kept overnight, added slowly with stirring into 50 cc. H2O and filtered after 2 hrs. gave 5.2 g. (crude) 3-methyl-6-trifluoromethyl-7-aminosulfonyl-1,2,4-benzothiadiazine 1,1-dioxide(IIIa), m. 334-6° (iso-PrOH). IIIa(1 g.) in 40 cc. Ac2O refluxed 5 hrs., filtered hot, and cooled gave 1.1 g. N-Ac derivative (IV) of IIIa, m. 298-300° (80% iso-PrOH) (decomposition). Similarly were prepared the following IVa (R and m.p. given): Et (V), 346-8° (decomposition); Pr, 318-20°; iso-Pr, 296-8° iso-Bu, 235-7°; C7H15, 203-5°; ClCH2, 312-14°; Cl2CH, 306-8°; CCl3, 293-5°; BrCH2, 292-4°; Br2CH, 258-60° MeCHBr,

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
306-8° (decompn.); Me2CHCHBr, 160-2°; Ph, 330-2°;
p-MeOC6H4, 290-2°; 3,4,5-(MeO)3C6H2, 228-30° (iso-PrOH);
p-MeC6H4, 280-2°; PhCH2, 164-6° (80% iso-PrOH); Ph2CH,
258-60° (iso-PrOH); EtPhCH, 237-9°; 2-pyridyl,
302-4°; 3-pyridyl, 334-6°; 4-pyridyl, 316-18°. IV (1
g.) refluxed 20 min. in 200 cc. H2O, filtered hot, and cooled gave 0.6 g.
IIIa, needles, m. 332-4° (80% iso-PrOH). V with Ac2O gave in the
usual manner the Ac deriv., m. 296-8°, which was hydrolyzed with
H2O to V, needles, m. 346-8°. IIIa (1 g.) and 30 cc. (EtCO)2O
refluxed 6 hrs. yielded 0.9 g. EtCO deriv. (VI) of IIIa, m. 284-6°
(decompn.) (80% iso-PrOH); V with (EtCO)2O gave similarly the EtCO deriv.
(VII) of IIIa, m. 280-2° (60% iso-PrOH). VI and VII refluxed with
dil. H2SO4 yielded IIIa. and V, resp.
IT 746-82-7, 4H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 859-25-6,
4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-p-tolyl-6-(trifluoromethyl)-,
1,1-dioxide 1550-90-9, 4H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(p-methoxyphenyl)-6-(trifluoromethyl)-, 1,1-dioxide 1691-04-9,
4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-(trifluoromethyl)-3-(3,4,5-
trimethoxyphenyl)-, 1,1-dioxide
(preparation of)
RN 746-82-7 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-phenyl-6-(trifluoromethyl)-,
1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

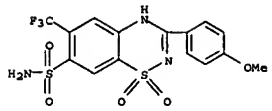


RN 859-25-6 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-p-tolyl-6-(trifluoromethyl)-,
1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

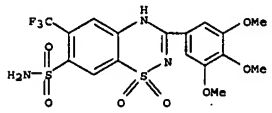


RN 1550-90-9 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-methoxyphenyl)-6-
(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

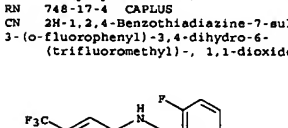


RN 1691-04-9 CAPLUS
CN 4H-1,2,4-Benzothiadiazine-7-sulfonamide, 6-(trifluoromethyl)-3-(3,4,5-
trimethoxyphenyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



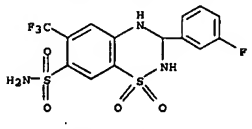
L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1963:33410 CAPLUS
DOCUMENT NUMBER: 58:33410
ORIGINAL REFERENCE NO.: 58:5689c-h,5690a
TITLE: A simple synthesis of dihydrobenzothiadiazine dioxide derivatives
AUTHOR(S): Klosa, Josef; Voigt, Hans
CORPORATE SOURCE: Privates Forschungslabor, Berlin-Zehlendorf
SOURCE: Journal fuer Praktische Chemie (Leipzig) (1962), 16, 264-76
CODEN: JPCEAO; ISSN: 0021-8383
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 58:33410
AB 6-Chloro- (I) and 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-2H-1,2,4-benzothiadiazine 1,1-dioxide (II) derivs., substituted at C-3 with R which was H, alkyl, aryl, or aralkyl, were synthesized by heating 2,4-disulfamoyl-5-chloroaniline (III) or the 5-trifluoromethyl analog (IV), resp., with RCHO (V) in aqueous HCl (EtOH added when III or IV were insol. in water). Nonaq. media were not necessary for the reaction. V which either reacted or did not react with III and IV were tabulated. Two mechanisms were discussed for the condensation reaction in aqueous media and one in nonaq. media. III (5.7 g.) was suspended in 150 ml. H2O, 0.02 mole V and 3 ml. concentrated HCl added, and if H2O-soluble addnl. 50 ml. H2O added, otherwise 50 ml. EtOH added, refluxed 40-60 min., and crystalline I filtered off hot. II were similarly prepared from IV. Acetals of halogenated V also condensed with III and IV to yield I and II, resp. Thus, 30 g. III was suspended in 80 ml. H2O and 50 ml. concentrated HCl, a solution of 18 ml. of the acetal of BrCH2CHO in 110 ml. EtOH added, the mixture refluxed 4 hrs., cooled, and the product filtered off and washed with H2O to yield 38 g. I (R = BrCH2) (VI), m. 224-6°. Similarly the acetals of Cl2CHCHO and ClCH2CHO yielded the corresponding I and II. I and II where R = 5-nitro-2-furyl were preferably prepared from 5-nitrofurfurel diacetate. The following I and II were prepared by the above routes (R and m.p. of I and II given): H, --, 261-3°; Me, 254-6°, 246-8°; Et, 266-8°, 262-4°; Pr, 255-7°, 228-30°; iso-Pr, 290-2°, 248-50°; Bu, 190-2°, 210-12°; iso-Bu, 244-6°, --; CH2Cl, 234-6°, 237-9°; CHCl2, 242-4°, 244-6°; CCl3, 300-2°, --; CH2Br, 224-6°, 206-8°; CH2I (VII), 198-200°, 194-6°; PhCH2, 246-8°, 220-2°; PhCHMe, 220-4° (when recrystd. from EtOH yielded a soluble form, m. 226-8° and a slightly soluble form, m. 238-48°), 235-7°; PhCH:CH, 248-50°, 171-3°; 4-pyridyl, 326-8°, --; 2-furyl, 212-14°, 252-4°; 5-nitro-2-furyl, 220-2°, 212-14°; p-ClC6H4, 236-8°, 224-6°; p-O2NC6H4, 242-4°, 235-7°; p-ClC6H4CH2, 238-40°, 240-42°; p-MeOC6H4CH2, 224-6°, 245-7°; p-MeC6H4CH2, 230-2°, --; o-FC6H4, 245-7°, 243-5°; m-FC6H4, 223-5°, 248-50°; antipyryl, 244-6°, oil. VI (20 g.) and 16 g. KI in 200 ml. anhydrous Me2CO refluxed 5 hrs., half the solvent evaporated, and H2O added; 22 g. VII separated

L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
When, however, the reaction was carried out in H2O or EtOH only decompn. products were obtained. A suspension of 60 g. III, 2.6 l. H2O, 20 ml. concd. HCl, and 18 ml. 38% aq. HCHO (VIII) was stirred and refluxed 20-30 min. when all dissolved, the mixt. was refluxed 30 min., C added, and the mixt. filtered hot. From the filtrate sepd. on cooling 53 g. cryst. I (R = H) (IX), m. 270-2° (H2O). IX in hot 0.1N NaOH hydrolyzed to III. Excess VIII in the above reaction caused polymer formation. Thus, when a suspension of 5.7 g. III in 50 ml. H2O contg. 4 ml. 37% aq. VIII, 2 ml. concd. HCl, and 100 ml. EtOH was refluxed 1 hr., cooled, and 50 ml. H2O added 6 g. colorless resin (X), m. 265-70°, sepd., sol. in alcohols and other org. solvents. Polymer formation was avoided by carrying out the reaction in aq. NH3. Thus, a mixt. of 6.8 g. III, 40 ml. concd. aq. NH3, and 0.7-1 g. VIII (as the 37% aq. soln.) (or a large excess of VIII may also be employed) stirred and refluxed 20-30 min., decolorized with C, and filtered hot gave 4.5 g. IX, m. 270-2°. IX in 95% yield was also obtained after 1 hr. reflux of 57 g. III, 2.5 l. H2O, 20 ml. 25% NH3, and 30 ml. 37% aq. VIII. Mixed m.ps. of X with III or IX showed no depression, indicating that the wide range of m.ps. of IX reported (from III and gaseous HCl in nonaq. media) (Freeman and Wagner, CA 46, 1559i) was due to the presence of impurities in IX. The diuretic effects of I and II were tabulated and discussed.
IT 748-17-4, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(o-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
748-18-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(m-fluorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
748-19-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(p-chlorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
3872-12-6, 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3,4-dihydro-3-(p-nitrophenyl)-6-(trifluoromethyl)-, 1,1-dioxide
(preparation of)
RN 748-17-4 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(o-fluorophenyl)-3,4-dihydro-6-
(trifluoromethyl)-, 1,1-dioxide (8CI) (CA INDEX NAME)

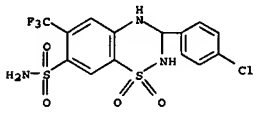


RN 748-18-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide,
3-(m-fluorophenyl)-3,4-dihydro-6-
(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

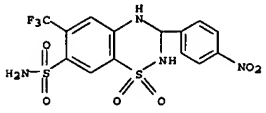
L4 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



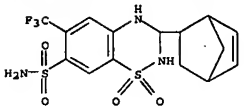
RN 748-19-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-(p-chlorophenyl)-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



RN 3872-12-6 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(p-nitrophenyl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)



L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



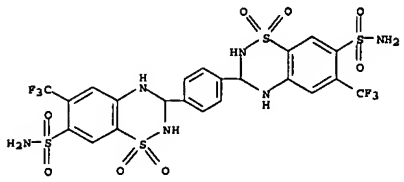
L4 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:423273 CAPLUS
DOCUMENT NUMBER: 57:23273
ORIGINAL REFERENCE NO.: 57:4685g-i,4686a-b
TITLE: 7-Sulfamoyl-3,4-dihydro- 1,2,4-benzothiadiazine 1,1-dioxides
INVENTOR(S): Mueller, Erich; Hasspacher, Klaus
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H.
SOURCE: 4 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 1125938		19620322	DE 1960-T17869	19600212
GB 906850			GB	

GI For diagram(s), see printed CA Issue.
AB The title compds. substituted in the 3 position with a bicyclic group were prepared by reaction of a 2,4-disulfamoylaniline with a bicyclic aldehyde or a functional derivative thereof. Thus, 8.5 g. 6,4,1,3-Cl(H2N)C6H2(SO2NH2)2 and 4.0 g. 2,5-endomethylene-1,2,5,6-tetrahydrobenzaldehyde in 25 cc. bis(2-methoxyethyl)ether was heated 2 hrs. at 100°, the solution left at room temperature 14 hrs., 50 cc. CHCl3 added, the precipitate filtered off, and dried to give 7.5 g. 3-(6-bicyclo[2.2.1]-2-heptenyl)-6-chloro-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (I), m. 129-30° (aqueous MeOH). I (6.0 g.) was hydrogenated in dioxane in the presence of Raney Ni to give 3-(6-bicyclo[2.2.1]heptyl) - 6 - chloro - 7 - sulfamoyl - 3,4 - dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 263-6°. Treatment of 4.0 g. I with 1.6 g. Br in AcOH gave 3.0 g. 3-[6-(2,3-dibromo)bicyclo[2.2.1]heptyl] - 6 - chloro - 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 199-201°. II prepared were (R, R1, R2, R3, R4, and m.p. given): H, 6-bicyclo[2.2.1]-2-heptenyl, H, CF3, H, 119° (AcOH-ligroine); H, 6-bicyclo[2.2.1]-2-heptenyl, Me, Cl, H, 190-1°; H, 6-bicyclo[2.2.1]-2-heptenyl, Cl, Cl, H, 184° (MeOHH2O); Me, 6-bicyclo[2.2.1]-2-heptenyl, H, Cl, Me, 232-5°; H, 6-bicyclo[2.2.1]-2-octenyl, H, Cl, H, 276-7°; H, 5-methylbicyclo[2.2.1]-2-hepten-6-yl, H, Cl, H, 197-9°. The compds. had stronger natriuretic activity than hydrochlorothiazid. Excretion of K was not increased to the same degree as that of Na.
IT 859-24-5, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (preparation of)
RN 859-24-5 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-yl)-6-(trifluoromethyl)-, 1,1-dioxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1962:7959 CAPLUS
DOCUMENT NUMBER: 56:7959
ORIGINAL REFERENCE NO.: 56:1537b-f
TITLE: Dihydrobenzothiadiazine. Diuretic activity of some new derivatives
AUTHOR(S): Selleri, Renato; Caldini, Oreste
CORPORATE SOURCE: Lab. Manetti & Roberts, Florence
SOURCE: Bollettino Chimico Farmaceutico (1961), 100, 323-9
CODEN: BCFAAI; ISSN: 0006-6648
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Cyclic derivs. of 4-amino-6-trifluoromethyl-m-benzenedisulfonamide (I) were synthesized by condensation with terephthalaldehyde (II), glyoxylic acid (III), phthalaldehydic acid (IV), pyruvaldehyde (V), phenylglyoxal (VI), and 4-biphenylylglyoxal (VII). I (6.4 g.) and 1.34 g. II in 30 cc. 1,2-dimethoxyethane with one drop concentrated H2SO4 were refluxed 2 hrs. and poured into 150 cc. H2O to give, after 24 hrs., p-bis(6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazin-3-yl)benzene, m. 300°. I (8 g.) and 8 g. III in 20 cc. H2O with 1 drop H2SO4 were refluxed 0.5 hr., cooled, and dissolved in aqueous NaHCO3 to give on acidification with dilute HCl 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazine-3-carboxylic acid (VIII), m. 238°. I (8 g.) and 3.75 g. IV in 50 cc. 1,2-dimethoxyethane with 1 drop H2SO4 were refluxed 2.5 hrs. and poured into 300 cc. H2O to yield 6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,1-dioxo-1,2,4-benzothiadiazine-(2,3:1',7')- or (3,4:1',7')benzopyrrolidinone, m. 323° (H2O). I (11 g.) and 11 g. V in 60 cc. H2O were refluxed for 1 hr. while adding 60 cc. 95% EtOH, then heated 1.5 hrs., and filtered. The residue was washed with EtOH and dried to give 3-acetyl-6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide, m. 285-7° (EtOH). Similarly, 16 g. I and 7.38 g. VI, refluxed 2 hrs., gave the 3-benzoyl derivative, m. 240-2°, and 16 g. I and 11.6 g. VII gave the 3-(p-phenylbenzoyl) derivative, m. 241°. VIII (0.75 g.) in 5 cc. EtOH, treated with 0.558 N-diethylaminoethyltheobromine in 5 cc. EtOH, gave the salt, m. 178° (decomposition). Similarly, the VIII-N-diethylaminoethyltheophylline, m. 195-8°, VIII-piperazine, m. 215-17°, and VIII-hexamethylenetetramine, m. 187°, salts were obtained. The compds. are useful as diuretics having an action equal to or stronger than dihydrofluomethiazide.
IT 1764-14-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (preparation of)
RN 1764-14-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1962:7744 CAPLUS
DOCUMENT NUMBER: 56:7744
ORIGINAL REFERENCE NO.: 56:1466h-i,1467a
TITLE: Bisbenzothiadiazine derivs
INVENTOR(S): Bernstein, Jack; Yale, Harry Louis
PATENT ASSIGNEE(S): Olin Mathieson Chemical Corp.
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3004024		19611010	US 1959-805374	19590410
PRIORITY APPLN. INFO.:			US	19590410

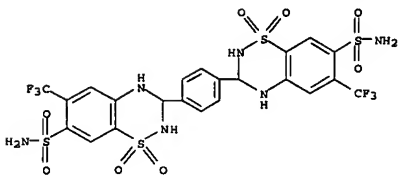
AB 3,3'-Bis(1,2,4-benzothiadiazine) 1,1-dioxide compds. (I), useful as diuretics and antihypertensives, containing particularly CF3 and sulfamoyl or N-substituted sulfamoyl groups in the benzenoid rings were prepared by condensation of a dicarbonyl, acetal, or ketal compound or a bis(dihalomethyl) derivative with a substituted o-aminobenzenesulfonamide. Thus, 31.9 g. 5-amino-α,α,α-trifluoro-2,4-toluenedisulfonamide was refluxed 4 hrs. with 4.3 g. succinaldehyde in 250 ml. 95% EtOH and 25 ml. 10% aqueous HCl, the EtOH distilled, and the residue, after slowly distilling on a steam-bath with 25 ml. 20% aqueous HCl and 100 ml. EtOH, filtered to give 20 g. of an ether-washed solid. Two recrystns. from 90% aqueous MeCN gave 3,3'-ethylenebis(3,4-dihydro-6-trifluoromethyl-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide), m. 257-9° (decomposition).

IT 1764-14-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (preparation of)

RN 1764-14-3 CAPLUS

CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,3'-p-phenylenebis[3,4-dihydro-6-(trifluoromethyl)-, 1,1,1',1'-tetraoxide (7CI, 8CI) (CA INDEX NAME)

L4 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1961:144261 CAPLUS
DOCUMENT NUMBER: 55:144261
ORIGINAL REFERENCE NO.: 55:27358f-i,27359a-i,27360a-b
TITLE: Diuretics. V. 3,4-Dihydro-1,2,4-benzothiadiazine 1,1-dioxides
AUTHOR(S): Whitehead, Calvert W.; Traverso, John J.; Sullivan, Hugh R.; Marshall, Frederick J.
CORPORATE SOURCE: Lilly Research Labs., Indianapolis, IN
SOURCE: Journal of Organic Chemistry (1961), 26, 2814-18
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 55:144261

AB The synthesis and properties of 30 new 3-cycloalkenyl and 3-cycloalkyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1, 1-dioxides were described. Correlations between their structures and biol. activity confirmed previously proposed analogies between similarly 3-substituted 3,4-unsatd. and 3,4-dihydro derivs. of the benzothiadiazine 1,1-dioxide nucleus. The following 1-cycloalkenylacetonitriles were prepared by a known method: 1-cycloheptenylacetonitrile, 81% yield, b11 104°, n25D 1.4808; 1-cyclopentenylacetonitrile, 64%, b10 72-3°, n25D 1.4672; 3-methyl-1(or 5)-cyclopentenylacetonitrile, 80%, b10 78°, n25D 1.4488; 2-methyl-1(or 5)-cyclopentenylacetonitrile, 79%, b11 83-4°, n25D 1.4672. 1-Cycloalkenylacetonitrile (0.8 mole) in 200 ml. alc. was hydrogenated at room temperature over 2 g. 5% Pd-C with H at 50 lb./sq. in. and the cycloalkyl acetonitrile distilled 3-Methylcyclopentylacetonitrile (97% yield) b10 79°, n25D 1.4411, and cycloheptylacetonitrile (88%) b10 102°, n25D 1.4654. A solution of 0.8 mole cycloalkylacetonitrile or cycloalkenylacetonitrile in 200 ml. dioxane and 400 ml. concentrated HCl refluxed 24-48 hrs., dioxane distilled in vacuo, the organic layer extracted with Et2O and then 2% NaOH, and the basic layer acidified gave the carboxylic acid, which was distilled to yield lactones of the 1-cycloalkenylacetic acids. Cycloheptylacetic acid (57% yield) b10 146-7°, and 1-cyclohexenylacetic acid (66% yield) b13 150-5°, n25D 1.4852. 1-Cyclopentenylacetic acid and 2-oxohexahydrocyclopenta[b]furan (I) [(approx. 1:1 mixture) (II)], obtained in 41% yield, n25D 1.4771, (64 g.) treated with SOCl2 gave 25.6 g. 1-cyclopentenylacetyl chloride, b10 88-100°. I was obtained in 55% yield, b10 118-20°. 3-Methylcyclopentylacetic acid(58%) b10 120-4°, n25D 1.4472. 2-Oxooctahydrocyclohepta[b]furan (70%) b10 146-50° and 2-oxo-4(or 6α)-methylhexahydrocyclopenta[b]furan (74%) b10 111-12°, n25D 1.4636. Mg (17.2 g.), 80 ml. Et2O, 10 g. 4-norbornylenylmethyl bromide, and a crystal of iodine treated (after the reaction started) with 121.8 g. more 5-norbornylenylmethyl bromide in 250 ml., Et2O added, and the mixture refluxed 1 hr., poured into dry ice in Et2O, acidified, and extracted gave 65.5 g. 5-norbornylenylacetic acid, b12 139°, n25D 1.4878. Cycloalkyl- and cycloalkenylacetic acids were converted to the acid chlorides with SOCl2. The amides were prepared in the usual manner: the acid chlorides were treated with PhNHMe or NHMe2 and C5H5N in C6H6, the solns. washed with H2O, dried, and evaporated and the amides distilled in vacuo.

The following RCH2CONMeR were thus obtained (R, R', % yield, b.p./ mm.

L4 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
given): 2-cyclopentenyl, Me, 79, 85°/0.25; 1-cyclohexenyl, Me, 75, 95°/0.4; cyclopentyl, Ph, 80, 130°/1; 1-cyclohexenyl, Ph, 80, 130°/0.3; 2-cyclohexenyl, Ph, 82, 130°/0.3; 3-cyclohexenyl, Ph, 90, 132°/0.3; cyclohexyl, Ph, 95, 136°/0.4; 3-methylcyclopentyl, Ph, 88, 104°/0.08; 5-norbornylenyl, Ph, 95, 117°/0.08; cycloheptyl, Ph, 95, 154°/1; 1-methylcyclohexyl, Ph, 98, 151°/4.5.
N-Methylcycloalkyl- or N-methylcycloalkenylacetanilides (1 mole) in 220 ml. tetrahydrofuran treated in 2 hrs. with 6.25 g. LiAlH4 suspended in 150-200 ml. tetrahydrofuran, the mixt. stirred overnight and treated with dil. alc., and the product distr. gave the aldehydes. The following compds. were obtained: 2-cyclopentenylacetaldehyde, 46.5%, b12 53-6°, n25D 1.4604; cyclopentylacetaldehyde, 55%, b12 53°, b. 156°; cyclohexylacetaldehyde, 45%, b15 68-70°, n25D 1.4615; 2-cyclohexenylacetaldehyde, 33%, b13 65°; 3-cyclohexenylacetaldehyde, 27%, b10 87-127°; 3-methylcyclopentylacetaldehyde, 44%, b12 63-6°, n25D 1.4421; 1-methylcyclohexylacetaldehyde, 39%, b11 82-5°, n25D 1.4619; cycloheptylacetaldehyde, 33%, b19 98-103°, n25D 1.4652; 5-norbornylenylacetaldehyde, 32%, b8 76-8°, n25D 1.4851. The following RCH2CH:NNHCONH2 were obtained (R and m.p. given): 2-cyclopentenyl, 116-17°; 3-cyclohexenyl, 142-4°; 3-methylcyclopentyl, 126-7°; cycloheptyl, 160-1°; 1-methylcyclohexyl, 170-1°. The following 2,4-(NO2)2C6H3NHN:CHCH2R were obtained (R and m.p. given): 2-cyclopentenyl, 98-9°; cyclopentyl, 128-9°; 2-cyclohexenyl, 97°; 3-methylcyclopentyl, 91-2°; 5-norbornylenyl, 124-5°; cycloheptyl, 96-7°. Li diethoxyaluminum hydride (0.156 mole) in Et2O was added in 0.5 hr. to 0.26 mole of the N,N-dimethylcycloalkenylacetamide in 200 ml. Et2O at 0-5°, the mixt. stirred 12 hrs. at room temp. and hydrolyzed with 2N H2SO4 at 0°, and the aldehyde-Et2O soln. washed, dried, and distd. in vacuo. 2-Cyclopentenylacetaldehyde was obained in 23% yield, b12 53°, and 1-cyclohexenylacetaldehyde in 17% yield, b2.5-3.5 53-64°.
4-Amino-6-chlorobenzene-1,3-disulfonamide (28.5 g.) in 400 ml. 50% 6N HCl and alc.; 31.9 g. 4-amino-6-trifluoromethylbenzene-1,3-disulfonamide in 200 ml. 50% 6N HCl and alc.; and 33 g. 4-amino-6-bromobenzene-1,3-disulfonamide in 300 ml. warm 50% 6N HCl and alc. suspensions were prepd. The appropriate aldehyde was added to each suspension and the mixt. shaken
0.5 hr., cooled after standing 12 hrs. at room temp., the product washed, and the resultant 3,4-dihydro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were dissolved in warm alc. and dild. with H2O. The product was recrystd. from dil. alc. The following 3,4-dihydro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxides were obtained (3 and 6 substituents, % yield, and m.p. given): 2-cyclopentenylmethyl, Cl, 71,222°; cyclopentylmethyl, Cl, 84, 230°; cyclopentylmethyl, Br, 80, 228°; hexylmethyl, Cl, 40, 172°; 2-cyclopentenylmethyl, CF3, 70, 148°; 2-cyclohexenylmethyl, Cl, 85, 221°; 2-cyclohexenylmethyl, Br, 80, 215°; 3-cyclohexenylmethyl, Cl, 35, 215°; 3-cyclohexenylmethyl, Br, 32, 202°; cyclopentylmethyl, CF3, 70, 156°; 1-cyclohexenylmethyl, Cl, 65, 225°; 3-methylcyclopentylmethyl, Cl, 80, 198°; 3-methylcyclopentylmethyl, Br, 80, 100°; cyclohexylmethyl, Cl, 85, 232°;

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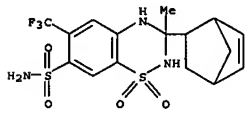
cyclohexylmethyl, Br, 80, 214°; 5-norbornylenyl, Cl, 40, 210°; 2-cyclohexenylmethyl, CF3, 86, 202°; 3-methylcyclopentylmethyl, CF3, 85, 185°; cycloheptylmethyl, Cl, 93, 215°; cycloheptylmethyl, Br, 76, 214°; 1-methylcyclohexylmethyl, Cl, 35, 245°; 5-norbornylenylmethyl, CF3, 76, 228°; cycloheptylmethyl, CF3, 60, 178°; 1-methylcyclohexylmethyl, CF3, 32, 190°; 2,3-dihydro-2-(γ-pyranyl), Cl, 30, 235°; 5-norbornylenyl, Cl, 46, 234°; 2-norbornyl, Cl, 80, 263°; 6-methylcyclohexenyl, Cl, 75, 230°; 6-methylcyclohexenyl, Br, 78, 230°; 6-methyl-5-norbornylenyl, Cl, 40, 235°. 6-Chloro-3-substituted-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide (0.1 mole) in 75 ml. tetrahydrofuran was treated with 1.5 g. NaBH4, treated dropwise with 1.5 g. AlCl3 in 50 ml. tetrahydrofuran, the mixt. refluxed 2 hrs., kept overnight, and decompd., and the solids sepd. and crystd. The following results were obtained (compd., % yield, and m.p. given): 6-chloro-3-cyclopentylmethyl-3,4-dihydro-7-(N-methylsulfamoyl)-1,2,4-benzothiadiazine 1,1-dioxide, 12, 174-5°; 6-chloro-3-cyclohexylmethyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, 60, -; 6-chloro-3-cyclopentylmethyl-3,4-dihydro-7-sulfamoyl-1,2,4-benzothiadiazine 1,1-dioxide, 40, -. The saluretic and diuretic activities of the compds. listed above were greater than those of the parent compd.
IT 1581-31-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-ylmethyl)-6-(trifluoromethyl)-, 1,1-dioxide (preparation of).
RN 1581-31-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-(5-norbornen-2-ylmethyl)-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)

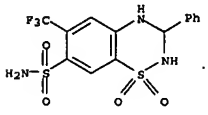


L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:105988 CAPLUS
DOCUMENT NUMBER: 55:105988
ORIGINAL REFERENCE NO.: 55:19971b-g
TITLE: Benzothiadiazine derivatives
INVENTOR(S): Lund, Frantz; Godtfredsen, Wagn O.
PATENT ASSIGNEE(S): Lovens Kemiske Fabrik ved. A. Kongsted
DOCUMENT TYPE: Patent
LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

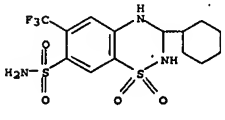
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 863474		19610322	GB	
DE 1226107			DE	
DK 97587			DK	
US 3254076		1966	US	
US 3254077		1966	US	

AB 6-Substituted 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (I), prepared from a substituted 2,4-disulfamoylaniline (II) and RCHO, H2C(OMe)2, or H2C:CHOR, had saluretic effects in rats and humans. Thus, a
solution of 3.2 g. 5-trifluoromethyl-2,4-disulfamoylaniline, 25 ml. EtOH, and
10 ml. ethylal, and a catalytic amount of p-MeC6H4SO3H was refluxed overnight and worked up to give the 6-trifluoromethyl derivative of I, m. 271-2°. By varying RCHO (or acetal) reactant, the following 3-substituted-6-trifluoromethyl analogs of I were prepared: Me (from EtOCH:
CH2, EtOCHClMe, or ClCH2CHO), m. 240-40.5°; ClCH2, m. 245-45.5;° BrCH2 (III), m. 209-10°; Et, m. 255-6°; Pr, 232-3°; iso-Pr, m. 244-5°; Bu, m.216-17°; δ-hydroxybutyl, m. 175-5.5°; n-pentyl, m. 190-1°; γ-nitropentyl, m. 243.5-5°; acetonyl, m. 208-9°; β-methoxyethyl, m. 188-90°; dicarbethoxymethyl, m. 232-4°; Ph, m. 218-19.5°; Ph2CH, m. 261-2.5°; p-methoxyphenethyl, m. 250-1.5°; benzyl (IV), m. 224-5°; phenethyl, m. 235-6°; α-phenylethyl (V), m. 243-4°; p-chlorobenzyl, 243-4°; benzyloxymethyl, m. 221-21.5°; phenoxymethyl, m. 244-6°; p-nitrophenoxymethyl, m. 261-2° (decomposition); p-aminophenoxymethyl, m. 193-4°; 2,4-dichlorophenoxymethyl, m. 230-1°; Bz, 261-2°; benzylthiomethyl, 202-3°; β-benzylthioethyl, 134-46°; 2-pyridyl, m. 304-6° (decomposition); 2-furyl, m. 190-2°; 3-cyclohexyl, m. 258-9°; 1-propenyl, m. 213-5°; n-hexyl, 178-9°; 3-pyridyl, m. 240-1°; styryl, m. 167-9°.
Substitution of a ketone for the aldehyde reactant yields the corresponding 3,3-disubstituted-6-trifluoromethyl analog of I; thus, acetone and 6-trifluoromethyl derivative of II gave the 3,3-dimethyl-6-trifluoromethyl derivative of I. The following were prepared similarly: 3-methyl-3-ethyl, m. 212-13°; 3-methyl-3-chloro (VI), m. 227-7.5°; 3-methyl-3-carbethoxy, m. 191-4°; 3-methyl-3-carbethoxymethyl, m. 150-2°; cyclopentane-1,3-spiro, m. 232-4°; cyclohexane-1,3-spiro, m. 261-2°; 2-chlorocyclohexane-1,3-spiro, m. 218-19°; 4-chlorocyclohexane-1,3-spiro (VII), m. 217-18°. By varying the 5-substituent in II, the following 3,3-dimethyl-6-substituted-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides were prepared: NO2, m. 233-3.5°; Cl (VIII), m. 230-1°; Br, m. 228-9°; MeO, m. 240-0.5°;

L4 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Me, m. 243-4°; H, m. 242-2.5°. The following were prepd. similarly. (substituents given): 3-Me, 3-Et, 6-Cl, m. 231-3°; 3-Me, 3-ClCH2, 6-NO2; 3-Me, 3-CO2Me, 6-NO2, m. 218-19°; cyclopentane-1,3-spiro-6-chloro, m. 234°; cyclohexane-1,3-spiro-6-bromo (IX), m. 281-3°; 2-methylcyclohexane-1,3-spiro-6-bromo, m. 231-3°; 2-chlorocyclohexane-1,3-spiro-6-chloro, m. 223-5°; 3-methyl-3-acetyl-6-chloro, m. 246-7°. Tests on groups of ten persons indicated that 2.0 mg. IV had the same saluretic effect as 20 mg. of the 6-Cl deriv. of I. III-IX were potent saluretic agents in rates.
IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 4454-81-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
(preparation of)
RN 1170-25-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 4454-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)

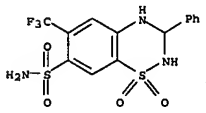


L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1961:39254 CAPLUS
DOCUMENT NUMBER: 55:39254
ORIGINAL REFERENCE NO.: 55:7664d-f
TITLE: Aromatic sulfamoyl compounds with diuretic action
AUTHOR(S): Lund, F. J.; Kobinger, W.
CORPORATE SOURCE: Research Labs. Leo Pharm. Prods., Copenhagen
SOURCE: Acta Pharmacologica et Toxicologica (1960), 16, 297-324
CODEN: APTOA6; ISSN: 0001-6683.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A relation was found between constitution and activity of substituted 2,4-disulfamoylanilines (DSA) and substituted 7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxides (DBT). DSA and DBT compds. showed a distinct relation between substitution in the benzene ring and saluretic activity. Substitution in the heterocyclic ring of DBT compds. yielded some substances considerably more potent than the known hydroflumethiazide (6-trifluoromethyl-7-sulfamoyl-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide) and hydrochlorothiazide. Of these substances, benzylhydroflumethiazide (Centyl) (the 3-benzyl derivative of hydroflumethiazide), which in human expts. showed the saluretic activity expected on the basis of the animal expts., was selected for further clin. use. Among the active substances studied, no differences in the urinary electrolyte-excretion pattern were detected by the method used.

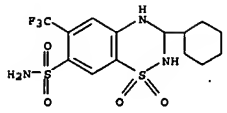
IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide 4454-81-3, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide
(as diuretic)

RN 1170-25-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)



RN 4454-81-3 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3-cyclohexyl-3,4-dihydro-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 8CI) (CA INDEX NAME)

L4 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



L4 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1960:11460 CAPLUS
DOCUMENT NUMBER: 54:11460
ORIGINAL REFERENCE NO.: 54:2351f-i,2352a-f
TITLE: Synthesis of trifluoromethylated compounds possessing diuretic activity
AUTHOR(S): Holdrege, Charles T.; Babel, Richard B.; Cheney, Lee C.
CORPORATE SOURCE: Bristol Labs., Inc., Syracuse, NY
SOURCE: Journal of the American Chemical Society (1959), 81, 4807-10
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 54:11460

AB Hydrated Na2S (113.5 g.) (containing 61% Na2S), 28.4 g. S, and 500 cc. H2O warmed on the steam bath to solution, the solution added dropwise with stirring to 400 g. 4,3-Cl(O2N)C6H3CF3 in 1.5 l. refluxing MeOH, refluxed 1 hr., cooled, and filtered yielded 359 g. [4,2-CF3(O2N)C6H3S]2 (I), m. 158-61° (AcOH). I (1000 g.) in 2.3 l. glacial AcOH and 250 cc. H2O treated 4 hrs. at 5-14° with gaseous Cl, heated 2 hrs. at 70°, cooled to 10°, chlorinated again 7 hrs., kept overnight, heated 0.5 hr. on the steam bath, and poured into 6 l. ice and H2O, the aqueous phase extracted with 1 l. PhMe, and the combined organic phase and extract evaporated gave crude 4,2-CF3(O2N)C6H3SO2Cl (II). The crude II added during 3 hrs. to 2 l. cold concentrated NH4OH below 15°, kept overnight, and filtered, the residue slurried with 4 l. 10% aqueous NaOH at 15°, filtered, acidified below 25°, cooled, and filtered, and the residue recrystd. from 2 l. iso-PrOH gave 490 g. 4,2-CF3(O2N)C6H3SO2NH2 (III), m. 165-7°; 2nd crop 66 g. A similar run with double the chlorination time yielded 54% III. III (5 g.) and 5 cc. glacial AcOH in 150 cc. H2O heated on the steam bath while being treated with 6 g. Fe filings in 2 portions 5 min. apart, stirred 3 hrs. on the steam bath, diluted with 100 cc. 95% EtOH, heated to boiling, filtered, neutralized hot with saturated aqueous Na2CO3, filtered, and cooled gave 3 g. 2-NH2 analog (IV) of III, m. 143-6° (aqueous EtOH). Fe filings (242 g.) added in portions during 1.5 hrs. to 242 g. NH4Cl, 190 g. III, 2 l. MeOH, and 1 l. H2O, the mixture refluxed 1.5 hrs., and filtered hot, the cake washed with 400 cc. MeOH, the combined filtrates diluted with 4.5 l. H2O, heated to boiling, filtered, and cooled to 0°, and the precipitate recrystd. from a mixture of 400 cc. H2O and 250 cc. MeOH containing 2 cc. 6N HCl yielded 126 g. IV, m. 141-5°. IV (35 g.) added during 0.5 hr. to 96 cc. ClSO3H with stirring and cooling, the mixture treated without cooling during 1 hr. with 87.6 g. NaCl, heated rapidly in a bath from 85 to 150°, kept 15 min. at 150°, and poured into 600 g. ice and H2O precipitated gummy 4,6,1,3-H2N(F3C)C6H2(SO2Cl)2 (V). The crude V added to 200 cc. concentrated NH4OH, kept overnight, heated on the steam bath, and cooled gave 15.7 g. 4,6,1,3-H2N(F3C)C6H2(SO2NH2)2 (VI), m. 239.5-41.5° (H2O). VI (1 g.) and 4 cc. 98% HCO2H refluxed 4 hrs., cooled, and filtered gave 7-sulfamoyl-6-trifluoromethyl-2H-1,2,4-benzothiadiazine 1,1-dioxide

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m. 300-2° (cor.) (1:1 95% EtOH-H2O). IV (45 g.) chlorosulfonated in the usual manner, 1/2 of the resulting V extd. with 125 cc. dioxane, the ext. treated with 15 cc. 40% aq. CH2O, kept at 10° overnight, basified with 125 cc. concd. NH4OH, kept 1.5 hrs. at room temp., heated 1 hr. on the steam bath, refluxed 2.5 hrs., cooled with ice, and filtered yielded 0.6 g. 3,4-dihydro deriv. (VIII) of VII, m. 260-4° (aq. EtOH). VI (63.8 g.), 16.5 g. 40% aq. CH2O, 300 cc. H2O, and 0.1 cc. concd. H2SO4 refluxed 3.5 hrs. with stirring, cooled, and filtered, and the residue recrystd. with 1.5 g. C from 400 cc. MeOH and 200 cc. H2O gave 43.5 g. VIII, m. 262-5°, 271-4° (cor.). Crude V from 22 g. IV added to 250 cc. 40% aq. MeNH2, kept overnight at room temp., and filtered, the filtrate concd., cooled, and filtered, and the residue dissolved in the min. amt. of MeOH at room temp. and repptd. with an equal vol. of H2O gave 11 g. 4,6,1,3-H2N(F3C)C6H2(SO2NHMe)2, m. 168-70° (H2O). VI (5 g.) and 45 cc. Me2C(OMe)2 refluxed 24 hrs. and evapd. gave 1.6 g. 3,3-di-Me deriv. of VII, m. 216-21° (aq. MeOH). VI (5 g.), 0.0173 mole appropriate aldehyde, 1 drop concd. H2SO4, and 30 cc. H2O refluxed, cooled, and filtered, and the residue recrystd. from Et2O aq. MeOH or aq. Me2CO gave the corresponding 3-substituted VII (IX); method A. VI (5 g.), 0.0173 mole appropriate aldehyde, and 30 cc. glacial AcOH refluxed and evapd. in vacuo, and the residue recrystd. from aq. MeOH gave the corresponding IX; method B. VI (5 g.), 0.0173 mole ethylene ketal of an appropriate cycloalkanone, 2 drops concd. H2SO4, and 50 cc. BuOH refluxed and evapd. in vacuo, and the residue recrystd. from aq. MeOH yielded the corresponding IX; method C. By these methods were prepd. the following IX (3-substituent, m.p., method, reactant, % yield, and reflux time given): Et, 262-3° (decompn.), A, EtCHO, 59, 4; Me, 247-50° (decompn.), A, AcH, 70, 0.25; PhCH2, 221-3°, B, PhCH2CHO, 35, 16; 2-pyridyl, 310-11°, A (without the H2SO4 catalyst), 2-C5H4NCHO, 19, 0.5; CCl3, 283-5° (decompn.), A, CCl3CH(OH)2, 22, 24; Ph, 220-4°, B, BzH, 17, 24; pentamethylene, 260-2°, C, cyclohexanone ethylene ketal, 23, 1.5; tetramethylene, 225-6° (decompn.), C, cyclopentanone ethylene ketal, 19, 2. VI and VII were potent orally active diuretics of low toxicity; VII was about 10 times as active orally as VI in animals.

IT 1170-25-8, 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide
(preparation of)

RN 1170-25-8 CAPLUS
CN 2H-1,2,4-Benzothiadiazine-7-sulfonamide, 3,4-dihydro-3-phenyl-6-(trifluoromethyl)-, 1,1-dioxide (6CI, 7CI, 8CI) (CA INDEX NAME)